latter material was dissolved in ether and washed with 5% sodium bicarbonate. Acidification of the bicarbonate extracts gave 1.1 g of recovered **2**. Redistillation of the neutral fraction gave 0.96 g of colorless oil, bp 77–80° (0.08 mm). Separation on column F at 120° gave, in order of elution, ester **15** (32% yield): ir (film) 1710 cm^{-1}; NMR ($CDCl_3$) τ 3.25 (1 H, m, br), 7.7–8.5 (9 H, m), 8.59 (6 H, s), and 9.09 (6 H, d, J = 7 Hz); mass spectrum m/e (rel intensity) 210 (0.2); 109 (30), 105 (100), and 84 (64). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.31; H, 10.76. Found: C, 74.17; H, 10.52. The second peak collected was identified as lactone **16**: ir (film) 1748 cm^{-1}; NMR ($CDCl_3$) τ 7.7 (1 H, d, br, J = 7 Hz), 8.0–9.1 (9 H, m), and 8.90, 8.95, 8.98, and 9.04 (all 3 H each, s); mass spectrum m/e (rel intensity) 210 (P, 3), 192 (22), 177 (12), 150 (51), 122 (39), 121 (32), 109 (100), and 99 (48). Anal. Found: C, 74.55; H, 10.65.

Irradiation of Methyl 2-Furoate (18) with 2,3-Dimethyl-2-butene. A solution of **18** (3.0 g) and DMB (30 g) in spectrograde hexane was irradiated for 9 hr. Evaporation of solvent and excess alkene gave a brown oil which gave on distillation 1.0 g of recovered **18** and 1.2 of a mixture of **19** and **20**. Separation was accomplished by GC on column D to give, first, oxetane **19** [ir (film) 1100 cm^{-1} (s, br); NMR ($CDCl_3$) τ 2.62 (1 H, 2 d, J = 2.0, 0.9 Hz), 3.58 (1 H, 2d, J = 2.4, 2.0 Hz), 3.66 (1 H, m), 6.95 (3 H, s), 8.60, 8.84, 9.09, and 9.15 (all 3 H, s); mass spectrum m/e (rel intensity 210 (0.2, P), 195 (1.4), 126 (48), 84 (100). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.58; H, 8.54. Found: C, 68.84; H, 8.40.] and second, [2 + 2] cycloadduct **20** [ir (film) 1732 cm^{-1}; NMR ($CDCl_3$) τ 3.67 (1 H, d, J = 28 Hz), 5.03 (1 H, t, J = 2.8 Hz), 6.62 (1 H, m), 6.97 (3 H, s), 8.75, 8.84, 8.92, and 9.10 (all 3 H, s); mass spectrum m/e (rel intensity) 210 (6, P), 195 (9), 151 (21), 126 (45), and 84 (100). Anal. Found: C, 68.39; H, 8.31.].

Acknowledgment. The author is grateful to Mr. William Landis of the National Institutes of Health for the mass spectra of the compounds reported herein.

Registry No.—**1**, 18448-47-0; **2**, 636-82-8; **3**, 1855-63-6; **5**, 54642-98-7; **7**, 54642-99-8; **8**, 54643-00-4; **9**, 54643-01-5; **11**, 54643-02-6; **12**, 54643-03-7; **13**, 54643-04-8; **15**, 54643-05-9; **16**, 54643-06-0; **17**, 18495-18-6; **18**, 611-13-2; **19**, 54643-07-1; **20**, 54643-08-2; 2-methyl-2-butene, 513-35-9; 2,3-dimethyl-2-butene, 563-79-1; furan, 110-00-9.

References and Notes

(1) For reviews, see (a) N. J. Turro in "Energy Transfer and Organic Photochemistry", N. J. Turro and P. Leermakers, Ed., Wiley-Interscience, New York, N.Y., 1974; (b) P. J. Wagner and G. S. Hammond, *Adv. Photochem.*, **5**, 1 (1968).
(2) G. M. J. Schmidt et al., *J. Chem. Soc.*, 1066, 2014 (1964), and references cited therein.
(3) D. R. Arnold, L. B. Gillis, and E. B. Whipple, *Chem. Commun.*, 918 (1969).
(4) For a review and references see R. O. Kan, "Organic Photochemistry", McGraw-Hill, New York, N.Y., 1966, pp 172–176, and references cited therein.
(5) (a) G. S. Hammond, C. A. Stout, and A. A. Lamola, *J. Am. Chem. Soc.*, **86**, 3103 (1964); (b) J. W. Hanifin and E. Cohen, *Tetrahedron Lett.*, 1419 (1966); (c) R. Hoffman, R. Wells, and H. Morrison, *J. Org. Chem.*, **36**, 102 (1971).
(6) O. L. Chapman and W. R. Adams, *J. Am. Chem. Soc.*, **89**, 4243 (1967); **90**, 2333 (1968).
(7) D. M. Gale, *J. Org. Chem.*, **35**, 970 (1970).
(8) M. J. Jorgenson, *Chem. Commun.*, 137 (1965).
(9) P. J. Kropp and H. J. Krauss, *J. Org. Chem.*, **32**, 3222 (1967).
(10) T. S. Cantrell, *J. Am. Chem. Soc.*, **95**, 2714 (1973).
(11) T. S. Cantrell, *J. Chem. Soc., Chem. Commun.*, 458 (1973).
(12) (a) T. S. Cantrell, *J. Am. Chem. Soc.*, **94**, 5929 (1972); (b) T. S. Cantrell, *J. Org. Chem.*, submitted for publication.
(13) Reference 1, pp 239–242.
(14) T. S. Cantrell, *Chem. Commun.*, 1656 (1970); *J. Org. Chem.*, **39**, 3063 (1974).
(15) T. S. Cantrell, *J. Org. Chem.*, **39**, 2242 (1974).
(16) L. A. Paquette, "Modern Heterocyclic Chemistry", W. A. Benjamin, New York, N.Y., 1968.
(17) For an exception, see P. J. Nelson, D. Ostrem, J. D. Lassila, and O. L. Chapman, *J. Org. Chem.*, **34**, 811 (1969).

Model Studies Directed toward the Total Synthesis of Vernolepin. III. Synthesis of the α-Methylene-δ-valerolactone AB Ring Model

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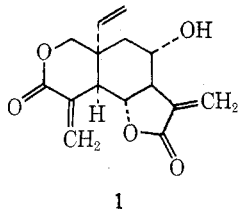
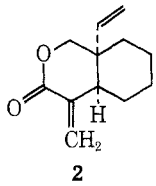
Two routes to the α-methylene-δ-valerolactone AB ring system (**2**) of vernolepin have been developed. The first approach involves a second-order Beckmann fragmentation on oxime **8**. The other approach employs an ozonolysis (reductive) of a Δ^2-enol acetate of an appropriately functionalized 3-ketodecalin. Introduction of the angular vinyl group in the latter approach is accomplished by facile elimination of the *o*-nitrophenyl selenoxide **20**. Introduction of the α-methylene unit involves α-hydroxymethylation of the enolate derived from lactone **3** followed by mesylation and β-elimination.

Our model studies directed toward the total synthesis of the growth-inhibitory sesquiterpene bislactone vernolepin (**1**)[3] have concentrated on the synthesis of the novel cis-fused AB ring system possessing an angular vinyl group. We wish to describe here the details of our model studies initiated a few years ago which led to the first synthesis of the vernolepin AB ring model **2**.[4] Several recent reports have described the synthesis of the δ-valerolactone system **3**[5–8] as well as its conversion to the α-methylene lactone **2**.[5]



1



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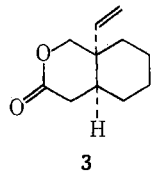

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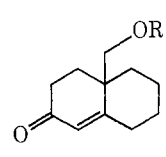
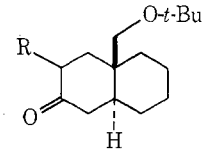
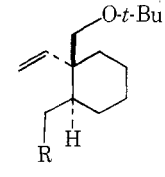


4, R = H
5, R = *t*-Bu



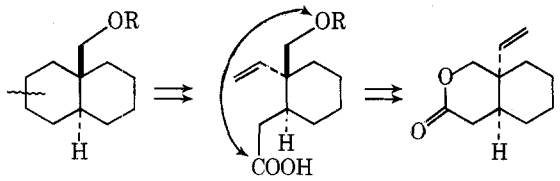
6, R = H
7, R = SCH_3



10, R = CN
11, R = COOH

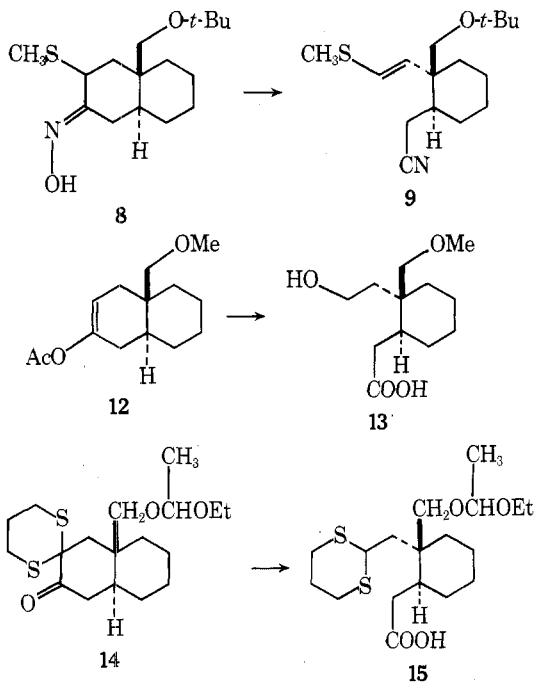
Our approach (see Scheme I) required a reaction or series of reactions which would allow for the specific cleavage of the C-2–C-3 bond (steroid numbering) of a suitably functionalized *trans*-decalin system with conversion of C-1 and C-2 into an olefin or potential olefin and formation of a carboxylic acid function or its equivalent at C-3. Such a carboxylic acid would upon lactonization provide the vernolepin cis-AB ring system possessing the angular vinyl

Scheme I



group. What would remain is a method for the introduction of the required α-methylene unit.

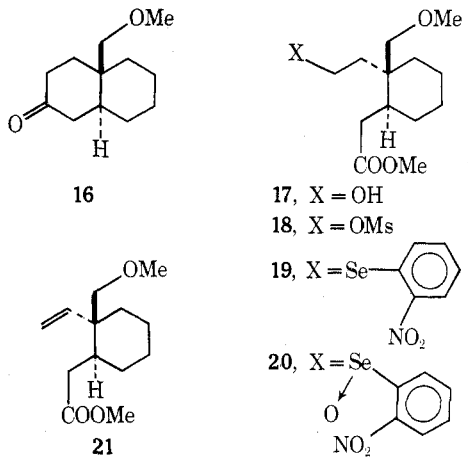
Several reaction schemes can be imagined for specific bond breaking of the C-2–C-3 carbon–carbon bond. In our hands the desired cleavage was carried out employing two approaches: a second-order Beckmann fragmentation[9] on the oxime of a 2-methylsulfenyl-3-keto decalin derivative (e.g., 8 → 9)[4] and ozonolysis (reductive) of the Δ^2-enol acetate derived from a 3-keto *trans*-decalin (e. g., 12 → 13).[8]



Both approaches meet the requirements stated above. Another approach developed by Marshall[6] involves base-induced C-2–C-3 carbon–carbon bond cleavage of the 3-keto dithiane derivative 14 (e.g., 14 → 15).

The required oxime 8 was prepared from the hydroxymethyl octalone 4[10] in the following manner. The hydroxymethyl group of 4 was protected as its *tert*-butyl ether. Metal–ammonia reduction of 5 afforded ketone 6. Formylation of decalone 6 followed by treatment with methyl thiotosylate[11] provided the methylsulfenyl decalone 7, which upon oximation yielded oxime 8. Addition of methanesulfonyl chloride to oxime 8 in refluxing pyridine resulted in cleavage of the desired C-2–C-3 bond with formation of 9. Cleavage of the carbon–sulfur bond of 9 followed by hydrolysis of the nitrile function would establish the first requirement stated above, namely, formation of an olefin between carbon atoms C-1 and C-2, and a carboxylic acid at C-3. Desulfurization with W-2 Raney nickel (deactivated) in ethanol yielded nitrile 10 in 90% yield. Hydrolysis of nitrile 9 afforded carboxylic acid 11 (85%), which upon treatment with *p*-toluenesulfonic acid in refluxing benzene resulted in a 95% yield of crystalline lactone 3.

An alternate approach to 3 involves the ozonolysis (reductive) of the Δ^2-enol acetate 12 which specifically cleaves the C-2–C-3 carbon–carbon bond establishing a carboxylic acid function at C-3 and a hydroxy group at C-2. The approach, however, is dependent upon a method for the conversion of the hydroxy ethyl side chain into the novel angular vinyl substituent (e.g., 17 → 21).

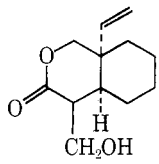


Cleavage of enol acetate 12 obtained from the hydroxymethyl decalone 16[12] with 1 equiv of ozone followed by reductive work-up with sodium borohydride–sodium hydroxide results in >95% yield of the hydroxy carboxylic acid 13. Attempts to eliminate alcohol 17 with formation of vinyl compound 21 via elimination of the corresponding primary alkyl phenyl selenoxide[13] resulted in a disappointingly low yield of olefin. However, attempts at converting 17 to 21 via elimination of the *o*-nitrophenyl selenoxide derivative 20 proved successful.[14] In a study on the elimination of a series of para- and ortho-substituted aryl alkyl selenoxides, Sharpless[15] observed that electron-withdrawing groups increased both the rate of the selenoxide elimination and the final yield of olefin.

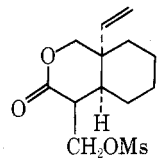
Mesylation of alcohol 17 afforded mesylate 18, which upon treatment with *o*-nitrophenylselenium anion (generated from di-*o*-nitrophenyl diselenide[16] and sodium borohydride in absolute ethanol) yielded selenide 19. Elimination of selenoxide 20 prepared by addition of 50% hydrogen peroxide to selenide 19 in tetrahydrofuran resulted in a 92% yield of vinyl compound 21. Cleavage of the methyl ether was executed with boron tribromide in methylene chloride at low temperature with simultaneous ring closure to the crystalline bicyclic δ-valerolactone 3, mp 44–45°, identical in all respects with the sample prepared above.

What remained was a method for the introduction of the desired α-methylene unit (e.g., 3 → 2). Despite considerable effort at the time we initiated our synthetic studies, the methods which had been developed for construction of the α-methylene function were unsatisfactory or not applicable to six-membered ring lactones.[17] Thus, we decided to develop a method which would prove useful for the construction of both α-methylene-γ- and -δ-lactone structural units.

We observed that both five- and six-membered ring lactones when treated with strong bases (e.g., lithium diisopropylamide) can be converted into their corresponding enolate anions and efficiently trapped with formaldehyde thus providing a ready route to α-hydroxymethyl-γ- and -δ-lactones.[18] Introduction of the α-methylene unit found in 2 was achieved via direct α-hydroxymethylation of lactone 3. The crude α-hydroxymethylated lactone 22 was converted into its corresponding mesylate (23) and thence (refluxing pyridine) to the bicyclic lactone 2 in 50% overall yield from 3. Heathcock has reported a synthesis of 2 employing the two-step α-hydroxymethylation procedure.[5]



22



23

Experimental Section

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Melting and boiling points are uncorrected. The following spectrometers were used: nuclear magnetic resonance (NMR), Varian T-60 and A-60D (in δ units, with Me_4Si as the internal reference in CCl_4 unless stated otherwise); infrared (ir), Perkin-Elmer Model 247; mass spectrometer (MS), LKB-9000 and Varian MAT CH5-DF. All reactions were performed under an atmosphere of nitrogen.

10-*tert*-Butoxymethyl-$\Delta^{1,9}$-2-octalone (5). Isobutylene (ca. 6 ml) was added to a solution of 10-hydroxymethyl-$\Delta^{1,9}$-2-octalone[10] (200 mg, 1.1 mmol) in methylene chloride (20 ml) containing concentrated sulfuric acid (0.1 ml) cooled to 0°. After stirring at 0° for 2 hr, the temperature was raised to 25° and maintained at that temperature for 16 hr. The reaction mixture was treated with saturated sodium bicarbonate solution, washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave a brown oil (236 mg) which was chromatographed on alumina. Elution with benzene afforded 206 mg (79%) of pure **5:** ir (film) 6.05, 6.19 μ; nmr (CCl_4) δ 1.20 (s, 9 H), 3.40 (s, 2 H), 5.64 (s, 1 H). Distillation [125° (bath temperature) (0.05 mmHg)] gave an analytical sample.

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.27; H, 10.17. Found: C, 76.33; H, 10.20.

9-*tert*-Butoxymethyl-*trans*-decalin-3-one (6). A solution of 5 (200 mg, 0.85 mmol) in dry tetrahydrofuran (8 ml) containing *tert*-butyl alcohol (63 mg, 0.85 mmol) was added to a solution of lithium metal (30 mg, 4.2 mmol) in liquid ammonia (80 ml). After refluxing for 40 min, the excess lithium was decomposed by very slow dropwise addition of methyl iodide just until the blue color disappeared. After evaporation of the liquid ammonia, water (10 ml) was added to the pasty residue. The product was extracted with ether. The combined ethereal extracts were washed with brine, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure to give an oil (206 mg). Purification by column chromatography on alumina (elution with benzene) gave 150 mg (75%) of pure **6:** ir (film) 5.85 μ; NMR (CCl_4) δ 1.2 (s, 9 H), 3.52 (s, 2 H), no olefinic hydrogens. The semicarbazone derivative (colorless needles, mp 204–205°, recrystallized from ethanol) was prepared for the analytical sample.

Anal. Calcd for $C_{16}H_{29}O_2N_3$: C, 65.08; H, 9.83; N, 14.24. Found: C, 64.94; H, 9.84; N, 14.08.

2-Methylsulfenyl-9-*tert*-butoxymethyl-*trans*-decalin-3-one (7). To a suspension of sodium hydride (4.0 g, 57% dispersion in mineral oil) in 60 ml of absolute benzene was added a mixture of decalone **6** (3.30 g, 13.9 mmol), ethyl formate (11.6 ml), and absolute methanol (5.6 ml) in 20 ml of benzene. The reaction mixture was stirred at room temperature for 48 hr. The reaction was quenched by the addition of ice water. The aqueous layer was separated, acidified with 10% hydrochloric acid, and extracted with ether. The combined ethereal extracts were washed with brine, dried over $MgSO_4$, and evaporated in vacuo. There was obtained 2.90 g (80%) of formyl ketone.

A solution of methyl thiotosylate[11] (1.89 g, 9.4 mmol) in absolute ethanol (10 ml) was added to a mixture of the above formyl ketone (2.40 g, 9.0 mmol) and potassium acetate (2.75 g) in absolute ethanol (110 ml). The mixture was refluxed for 38 hr. After evaporation of the solvent, the product was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate, and evaporated to give a dark brown oil which was purified by column chromatography (silic gel–benzene) to give analytically pure **7** (1.35 g, 53%): mp 62°; ir ($CHCl_3$) 5.85 μ; NMR (CCl_4) δ 1.18 (s, 9 H), 2.00 (s, 3 H), 3.43 (q, 1 H). An analytical sample was prepared by recrystallization from petroleum ether (colorless prisms, mp 62–63°).

Anal. Calcd for $C_{16}H_{28}O_2S$: C, 67.61; H, 9.86. Found: C, 67.87; H, 9.97.

Fragmentation of Oxime 8. A mixture of ketone **7** (960 mg, 3.38 mmol), hydroxylamine hydrochloride (750 mg), and sodium hydroxide (500 mg) in 95% aqueous ethanol (40 ml) was refluxed for 2 hr. After evaporation of the solvent, the product was extracted with ether. The ethereal extracts were washed with brine, dried over $MgSO_4$, and evaporated to give 1.01 g (quantitative) of oxime **8.**

Methanesulfonyl chloride (1.16 g, 10.1 mmol, freshly distilled) was added to a solution of crude oxime **8** (1.01 g, 3.37 mmol) in dry pyridine (15 ml). The mixture was refluxed for 1.5 hr. The product was extracted with ether. The combined ether layers were washed with 10% hydrochloric acid, saturated sodium bicarbonate, and brine. After drying ($MgSO_4$) and removal of the solvent in vacuo there was obtained 1.04 g of crude material which was chromatographed on silica gel. Elution with benzene gave 430 mg (45%) of pure nitrile **9:** ir (film) 4.48, 6.17, 10.68 μ (trans-substituted enol thioether); NMR (CCl_4) δ 1.20 (s, 9 H), 2.20 (s, 3 H), 3.30 (AB q, 2 H), 5.62 (AB q, J = 16 Hz, 2 H). An analytical sample was prepared by distillation [140° (bath temperature) (0.1 mmHg)].

Anal. Calcd for $C_{16}H_{27}NOS$: C, 68.27; H, 9.67; N, 4.98. Found: C, 68.43; H, 9.76; N, 5.25.

2-Vinyl-*cis*-2-*tert*-butoxymethylcyclohexylacetonitrile (10). A suspension of nitrile **9** (130 mg) and W-2 Raney nickel (2 ml, deactivated by refluxing in acetone for 3 hr) in ethanol (20 ml) was refluxed for 4 hr. Filtration of the Raney nickel afforded a filtrate which gave upon removal of the solvent 110 mg of crude **10** as a pale yellow oil. Column chromatography on silica gel (benzene) yielded 100 mg (90%) of pure **10.** An analytical sample was prepared by distillation [100–105° (bath temperature) (0.1 mmHg)]: ir (film) 3.24, 4.48, 6.12, 10.95 μ; NMR (CCl_4) δ 1.20 (s, 9 H), 3.30 (AB q, 2 H), 4.80–5.95 (m, $CH{=}CH_2$, 3 H).

Anal. Calcd for $C_{15}H_{25}NO$: C, 76.55; H, 10.71; N, 6.38. Found: C, 76.60; H, 10.65; N, 6.17.

9-Vinyl-2-oxa-*cis*-3-decalone (3). A mixture of **10** (1.00 g) and potassium hydroxide (12.0 g) in diethylene glycol (11 ml) and water (9 ml) was refluxed for 10 hr. After cooling, water (40 ml) was added and the mixture was washed with ether. The aqueous layer was acidified with concentrated hydrochloric acid. The product was extracted with ethyl acetate. The combined ethyl acetate extracts were washed with water, dried over magnesium sulfate, and evaporated in vacuo to give 920 mg (85%) of acid **11,** ir (film) 2.74–4.10, 5.86 μ.

A solution of acid **11** (513 mg) in benzene (150 ml) was refluxed in the presence of *p*-toluenesulfonic acid (100 mg) with azeotropic removal of water (Dean-Stark apparatus) for 19 hr. The reaction mixture was washed with saturated sodium bicarbonate solution and brine. After drying ($MgSO_4$) and removal of the solvent under reduced pressure there was obtained 345 mg (95%) of lactone **3** (colorless prisms, mp 44–45°): ir ($CHCl_3$) 5.79, 6.12, 10.90 μ; NMR (CCl_4) δ 5.16–5.68 (m, $CH{=}CH_2$, 3 H), 4.14 (AB q, OCH_2–, 2 H). An analytical sample was prepared by recrystallization from petroleum ether, mp 44–45°.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.33; H, 8.89. Found: C, 73.30; H, 9.01.

α-Methylene-δ-valerolactone (2). *n*-Butyllithium (0.51 ml of a 1.60 *M* solution in hexane) was added to a solution of diisopropylamine (83 mg, 0.82 mmol) in dry THF (5 ml) cooled to −78°. After 30 min, a solution of lactone **3** (122 mg, 0.68 mmol) in dry THF (2 ml) was added dropwise over a period of 15 min. The reaction mixture was allowed to stir for 30 min at −78°. Then the temperature was raised to −25° and formaldehyde [generated by heating paraformaldehyde (0.4 g) at 150°] was passed into the reaction vessel with the aid of a stream of nitrogen. After complete depolymerization the reaction mixture was stirred for an additional 30 min at −25°. The reaction was quenched by the addition of 10% hydrochloric acid. The product was extracted with ether. The combined ether extracts were washed with brine, dried over $MgSO_4$, and condensed to give 144 mg of crude **22.** This crude product was used directly in the next reaction.

A solution of **22** (144 mg) and methanesulfonyl chloride (156 mg) in pyridine (4.5 ml) was allowed to stir at room temperature for 20 hr. The product was extracted with ethyl acetate. The ethyl acetate layers were washed with water and dried over anhydrous magnesium sulfate. Removal of the solvent gave 200 mg of crude mesylate **23** as a yellow oil. This material was used immediately in the next reaction.

A solution of mesylate **23** (200 mg) in pyridine (3.6 ml) was refluxed for 5 hr. The product was extracted with ether. The combined ethereal extracts were washed with water, dried over $MgSO_4$, and condensed in vacuo to give 100 mg of an oil. Chromatography on silica gel (hexane–ether, 1:1) gave pure α-methylene lactone **2** (60 mg, 46%): ir ($CHCl_3$) 5.84, 6.10, 6.17 μ; NMR (CCl_4) δ 6.34 (s, 1 H), 5.44 (s, 1 H), 5.00–5.80 (m, $CH{=}CH_2$, 3 H), 4.12 (AB

2, 2 H). An analytical sample was prepared by distillation [100° (bath) (0.2 mmHg)].

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 74.69; H, 8.40

Methyl 2-Methoxymethyl-*trans*-2-β-hydroxyethylcyclohexylacetate (17). A solution of enol acetate **12** [1.5 g, 6.3 mmol (prepared from **16**,[12] isopropenyl acetate, $TsOH \cdot H_2O$, reflux, 24 hr)[19]] in 30 ml of methylene chloride cooled to −78° was treated with ca. 1 equiv of ozone. After ozone addition was complete, 30 ml of methanol was added at −78° to the reaction mixture followed by sodium borohydride (269 mg). An equal amount of sodium borohydride was added every 15 min for approximately 1 hr (−78°). After all the sodium borohydride was added, the reaction was warmed to room temperature and was treated with 11.4 ml of 1.0 *N* aqueous sodium hydroxide. After ca. 30 min, the solvents were evaporated under reduced pressure and the residue was taken up in a minimum amount of water and washed with ether (15 ml). The aqueous layer was cooled (5°), treated with 5% hydrochloric acid until acidic, and extracted with chloroform. The combined chloroform extracts were dried over magnesium sulfate and evaporated in vacuo, affording 1.4 g (97%) of acid **13**: ir (film) 5.86 μ; NMR ($CDCl_3$) δ 3.35 (s, 3 H, OMe), 3.68 (t, 2 H, CH_2OH); MS *m/e* 230.

The above carboxylic acid (628 mg) in ether was treated with diazomethane, affording 609 mg of crude ester **17**. Chromatography on silica gel (30 g) (elution with hexane–ethyl acetate, 1:1) gave 550 mg (83%) of pure methyl ester **17**: ir ($CHCl_3$) 2.95, 2.80 μ; NMR (CCl_4) δ 3.59 (s, 3 H, COOMe), 3.30 (s, 3 H, OMe); MS *m/e* 244. An analytical sample was prepared by distillation [130° (bath temperature) (0.15 mmHg)].

Anal. Calcd for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.73; H, 9.87.

Methyl 2-Methoxymethyl-*trans*-2-β-mesyloxyethylcyclohexylacetate (18). Methanesulfonyl chloride (56 μl, 0.74 mmol) (freshly distilled) was added to a solution of ester alcohol **17** (130 mg, 0.52 mmol) in 1.5 ml of anhydrous pyridine cooled to 0°. The reaction mixture was stirred at room temperature for 30 min. The reaction mixture was taken up in ether and washed with cold 5% hydrochloric acid and brine. The ether layer was dried (anhydrous magnesium sulfate) and the solvent was removed under reduced pressure, providing 154 mg (96%) of crude mesylate **18**: ir (film) 5.80 7.41, 8.55 μ; NMR (CCl_4) δ 4.22 (t, J = 7 Hz, 2 H, CH_2OMs), 3.59 (s, 3 H, COOMe), 3.25 (s, 3 H, OMe), 2.90 (s, 3 H, $-SO_2Me$).

Methyl 2-Methoxymethyl-*trans*-2-vinylcyclohexylacetate (21). To a suspension of di-*o*-nitrophenyl diselenide (64 mg, 0.16 mmol) in absolute ethanol (0.5 ml) at room temperature was added sodium borohydride (12 mg, 0.32 mmol). After approximately 30 min, the reaction mixture became homogeneous (deep red color). To the selenium anion cooled to 0° was added the crude mesylate **18** (100 mg, 0.30 mmol) in 0.5 ml of absolute ethanol. After addition was complete, the reaction mixture was stirred for 14 hr at room temperature. The reaction mixture was taken up in ether, washed with water, and dried over $MgSO_4$. Removal of the solvent in vacuo afforded the crude selenide, which was purified by preparative thin layer chromatography (silica gel plates). Elution with hexanes–ether (2:1) gave 74 mg (64%) of pure selenide **19**: ir (film) 5.80, 6.62, 7.51 μ; NMR (CCl_4) δ 8.18 (d, 1 H), 7.38 (m, 3 H), 3.58 (s, 3 H), 3.30 (br s, 5 H, CH_2OCH_3), 2.81 (t, 2 H, CH_2Se).

A solution of *o*-nitrophenyl selenide **19** (74 mg, 0.17 mmol) in anhydrous tetrahydrofuran (1.0 ml) cooled to 0° was treated with 50% hydrogen peroxide (47 μl). After addition was complete, the temperature was raised to 25° and maintained at that temperature for 12 hr. The reaction mixture was taken up in ether followed by washing of the organic layer with water and brine. The organic layer was dried (anhydrous magnesium sulfate) and the solvent was removed under reduced pressure, leaving 42 mg of crude olefin **21**. Purification by column chromatography (elution with hexanes–ether, 4:1) gave 36 mg (92%) of pure **21**: ir ($CHCl_3$) 5.79, 6.13, 10.00, 10.90 μ; NMR (CCl_4) δ 4.8–6.0 (typical vinyl pattern, 3 H), 3.58 (s, 3 H, COOMe), 3.25 (br s, 5 H, CH_2OCH_3); MS *m/e* 226.

Anal. Calcd for $C_{13}H_{22}O_3$: 226.1569. Found: 226.1561.

9-Vinyl-2-oxa-*cis*-decalin-3-one (3). The methoxymethyl ester **21** (30 mg, 0.13 mmol) in dry methylene chloride (1.0 ml) cooled to −78° was treated with boron tribromide (93 μl, 0.79 mmol). After addition was complete, the temperature was raised to −20° and kept at that temperature for 30 min, followed by warming to 0°. Stirring was continued for 1 hr at 0°. The reaction was quenched by the addition of 2.0 ml of ether at 0° followed by the addition of aqueous sodium bicarbonate solution. When carbon dioxide evolution ceased, the product was extracted with ether. The combined ether extracts were washed with brine and dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave 30 mg of crude material which was purified by passage through a column of silica gel (2.0 g). Elution with hexanes–ether (2:1) gave 21 mg (88%) of crystalline **3**, mp 44–45°, identical in all respects (melting point, mixture melting point, TLC, ir, NMR, MS) with a sample previously prepared in our laboratory.[4]

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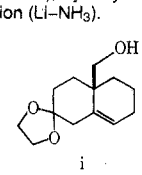
Registry No.—**2**, 42391-68-4; **3**, 42391-78-6; **4**, 18992-92-2; **5**, 42391-70-8; **6**, 42391-71-9; **6** semicarbazone, 42391-72-0; **7**, 42391-73-1; **8**, 42391-74-2; **9**, 42391-75-3; **10**, 42391-76-4; **11**, 42391-77-5; **12**, 54549-34-7; **13**, 54549-35-8; **17**, 54549-36-9; **18**, 54667-58-2; **19**, 54549-37-0; **21**, 54549-38-1; isobutylene, 115-11-7; *tert*-butyl alcohol, 75-65-0; methyl thiotosylate, 4973-66-4; methanesulfonyl chloride, 124-63-0.

References and Notes

(1) Fellow of the Alfred P. Sloan Foundation, 1974–1976.
(2) Research Fellow of the Universidad Nacional Autonoma de Mexico, 1974–1975.
(3) S. M. Kupchan, R. J. Hemingway, D. Werner, A. Karim, A. T. McPhail, and G. A. Sim., *J. Am. Chem. Soc.*, **90**, 3596 (1968); S. M. Kupchan, R. J. Hemingway, D. Werner, and A. Karim, *J. Org. Chem.*, **34**, 3903 (1969).
(4) P. A. Grieco and K. Hiroi, *Tetrahedron Lett.*, 1831 (1973).
(5) R. D. Clark and C. H. Heathcock, *Tetrahedron Lett.*, 1713 (1974).
(6) J. A. Marshall and D. E. Seitz, *Syn. Commun.*, **4**, 395 (1974).
(7) S. Danishefsky, 9th International Symposium on the Chemistry of Natural Products, Ottawa, Canada, June 24–28, 1974, Abstract 29G.
(8) P. A. Grieco, J. J. Reap, and J. A. Noguez, *Syn. Commun.*, **5**, 155 (1975).
(9) R. L. Autrey and P. W. Scullard, *J. Am. Chem. Soc.*, **90**, 4924 (1968). For application of the second-order Beckmann fragmentation to natural product synthesis see R. L. Autrey and P. W. Scullard, *J. Am. Chem. Soc.*, **90**, 4917 (1968); Y. Shimizu, *Tetrahedron Lett.*, 2919 (1972).
(10) L. S. Minckler, A. S. Hussey, and R. H. Baker, *J. Am. Chem. Soc.*, **78**, 1009 (1956).
(11) D. T. Gibson, *J. Chem. Soc.*, 2637 (1931).
(12) Prepared in 95% overall yield from the hydroxymethyl ketal i[10] via methylation (NaH–THF–MeI), hydrolysis (acetone–TsOH, room temperature, 2 hr), and reduction (Li–NH_3).



i

(13) K. B. Sharpless, M. W. Young, and R. F. Lauer, *Tetrahedron Lett.*, 1979 (1973).
(14) For an application of the *o*-nitrophenyl selenoxide elimination to natural product synthesis (moenocinol), see P. A. Grieco, Y. Masaki, and D. Boxler, *J. Am. Chem. Soc.*, **97**, 1597 (1975).
(15) K. B. Sharpless and M. W. Young, *J. Org. Chem.*, **40**, 947 (1975).
(16) H. Bauer, *Ber.*, **46**, 92 (1913).
(17) For a review of α-methylene lactone synthesis see P. A. Grieco, *Synthesis*, 67 (1975).
(18) P. A. Grieco and K. Hiroi, *J. Chem. Soc., Chem. Commun.*, 1317 (1972).
(19) R. Villotti, H. J. Ringold, and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 5693 (1960).