impedance of electrophile approach by the *gem*-dimethyl bridge, and (iii) development of tetrahedral character at C_4 with approach trans to the *gem*-dimethyl bridge displaces the C_4-methyl group toward the congested region of this bridge. In the case of *trans*-verbenylstannane, factor i is opposed by ii, but in the cis isomer i is opposed by iii. The outcome thus depends on the relative importance of these factors, and the production of comparable amounts of *cis*- and *trans*-δ-pinenes from each isomer suggests that the major influence directing γ-proton addition is the *gem*-dimethyl bridge but that in the *cis*-stannane isomer this is reinforced by the inherent γ-anti preference, leading to ca. 80% *cis*-δ-pinene. That acidolysis of *cis*-stannane does not produce solely *cis*-δ-pinene (anti attack) (cooperative effect of factors i and ii indicates the significance of factor iii. Work currently underway in other bicyclic systems should provide more insight into the relative importance of factors influencing the stereochemistry of S_E' processes, particularly where exo,endo and syn-anti competition can be examined.

Experimental Section

Compounds. Predominantly *trans*-verbenol was obtained as described by Whitham[7] and converted to the **verbenyl chlorides** with either thionyl chloride or *N*-chlorosuccinimide/dimethyl sulfide as described previously[3] for cyclohex-2-enol. The chlorides were fully characterized by their ^{13}C and ^1H NMR spectra (Tables I and II). Anal. Calcd for $C_{10}H_{15}Cl$: C, 70.4; H, 8.9. Found: C, 70.9; H, 9.0.

Trimethylstannylation, employing $(CH_3)_3SnLi$ in tetrahydrofuran, was conducted as described previously.[3] Thus treatment of a 93:7 trans/cis verbenylchloride sample with $(CH_3)_3SnLi$ provided the stannane mixture described in the text in ca. 67% yield after Kugelrohr distillation (2 mmHg, oven temperature 120 °C). Anal. Calcd for $C_{13}H_{24}Sn$: C, 52.2; H, 8.1. Found: C, 51.4; H, 8.0. The ^{119}Sn, ^1H, and ^{13}C NMR spectra of the stannanes are described in the text and/or summarized in Tables I and II.

Triphenylstannylation of the verbenyl chlorides was conducted with an excess (1.5 equiv) of (triphenylstannyl)lithium in tetrahydrofuran as described previously. The crude product was dissolved in warm ethanol in which hexaphenylditin was very poorly soluble. The required stannane (60%) formed a very viscous oil. Anal. Calcd for $C_{28}H_{30}Sn$: C, 69.3; H, 6.2. Found: C, 70.2; H, 6.8. The ^{119}Sn, ^1H, and ^{13}C NMR spectra are described in the text. *cis*- and *trans*-δ-pinenes were kindly provided by Professor G. Zweifel and were fully characterized by ^1H and ^{13}C NMR and combined GC-MS.

Reactions with sulfur dioxide in chloroform or methanol and trifluoroacetic acid ($CDCl_3$) were conducted directly in 10-mm NMR tubes. The reaction products were examined directly by NMR spectroscopy and combined gas chromatograph-mass spectrometry (and comparison with authentic samples) where appropriate.

Acknowledgment. We are grateful to the Australian Research Grants Scheme for partial funding of this research. Prof. G. Zweifel (Unversity of California, Davis) kindly made available samples of authentic *cis*- and *trans*-δ-pinenes.

Synthetic Studies Aimed at the Dolastanes. An Attempted A + C → ABC Approach

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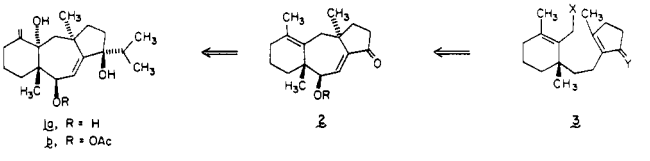
The dolastanes are marine diterpenes whose molecular array of fused 6-7-5 alicyclic rings is distinctive. As part of a program directed toward the synthesis of representatives of these bioactive natural products, the possibility of elaborating their framework by intramolecular cyclization to form the central seven-membered ring has been examined. An expedient two-step route to keto ester **8** was developed. This intermediate proved receptive to copper-promoted conjugate addition of allylmagnesium bromide and [(*E*)-2-(trimethylsilyl)vinyl]lithium. The acetal **21** to be subsequently derived from these adducts could be conveniently crafted into the highly functionalized 2-cyclopentenones **27**. Central to the synthetic strategy was the need for intramolecular C-C bond formation within **27**. Because we were singularly unsuccessful in achieving the desired end result, this particular approach appears unsuited for gaining access to the dolastanes.

The dolastane family consists of a small group of tricyclic diterpenes of marine origin having a uniquely distinctive linear 6-7-5 array of fused alicyclic rings. Dolatriol (**1a**) and its 6-acetate (**1b**) were the first members to be characterized.[2] Of particular note are the impressive cytotoxic properties of **1a**, which markedly inhibits the growth of P-388 lymphocytic leukemia. The location of its three allylic hydroxyl groups and the relative stereochemistry of its five stereogenic centers were defined by three-dimensional X-ray analysis of **1b**.[3] To this time, no reports have appeared describing efforts aimed at the preparation of this class of diterpenes. Our first attempts to assemble the tricyclic nucleus of **1** took the form of the socalled A + C → ABC route. Key compounds in this retrosynthetic analysis are suitably activated derivatives of the bicyclic diene **3**. Although lacking in precedent, the expectation was that bond formation could be achieved within **3** under the proper anionic or cationic conditions,



1a, R = H
1b, R = OAc
2
3

perhaps with good stereocontrol at the site of the incipient

(1) Kimberly Graduate Fellow, 1984-1985.
(2) Pettit, G. R.; Ode, R. H.; Herald, C. L.; Von Dreele, R. B.; Michel, C. *J. Am. Chem. Soc.* **1976**, *98*, 4677.
(3) Von Dreele, R. B. *Acta Crystallogr. Sect. B: Struct. Sci.* **1977**, *B33*, 1047.

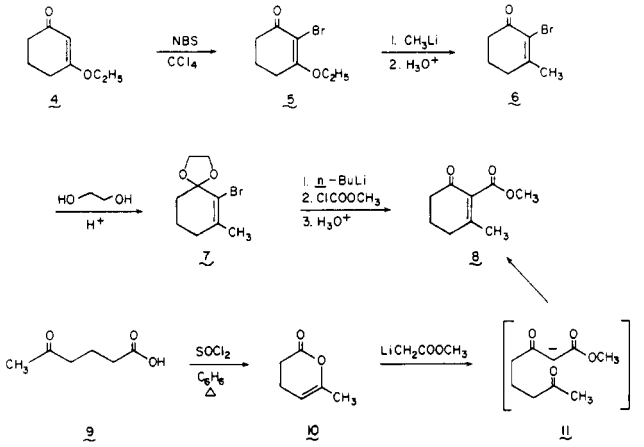
0022-3263/85/1950-4102$01.50/0

angular methyl group. Following adjustment of oxidation level and arrival at **2**, suitably directed entry of the isopropyl substituent was anticipated. Singlet oxygenation of the methylcyclohexene A ring[4] would complete the task.

This paper develops a strategy for gaining access to substrates of type **3**. Also presented are several fundamental complications associated with the specific cyclization highlighted in the retrosynthetic plan.

Results and Discussion

β-Keto ester **8** was viewed as an attractive starting material since three easily distinguishable electrophilic centers are incorporated therein. Its preparation began by bromination of **4** with *N*-bromosuccinimide followed by exposure of **5** to methyllithium.[5,6] The ensuing acquisition of ketal **7** prompted scrutiny of its metalation[7-9] and capture of the derived vinyl anion with methyl chloroformate.[10] However, this sequence provided **8** in a maximum yield of only 15%. This less than satisfactory outcome probably has its origins in the steric blockade provided by the C-3 methyl group and the acidic protons offered by this substituent.[11]

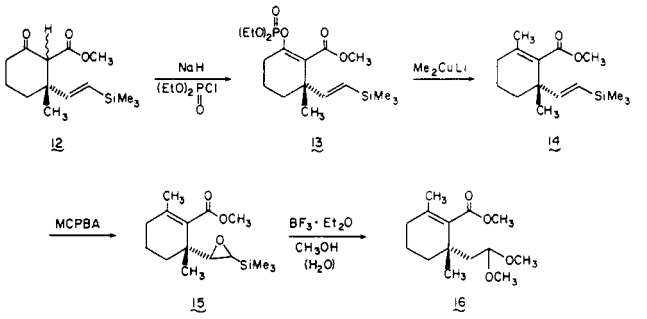


4 **5** **6** **7** **8** **9** **10** **11**

A far more expedient synthesis of **8** was subsequently uncovered. Heating commercially available 4-acetylbutyric acid (**9**) with thionyl chloride in benzene delivered lactone **10**.[12] The latter was condensed with methyl α-lithioacetate[13] in tetrahydrofuran solution at −78 °C. The initial ring-opened product **11** underwent cyclization and dehydration during the warming and acidic workup.[14] Compound **8**, obtained in 32% overall yield via this two-step procedure, is now regarded as readily available.

With an adequate supply of **8** in hand, the task of appending a masked aldehyde equivalent at its β carbon was undertaken. When ((*Z*)-2-ethoxyvinyl)lithium[15] could not be coaxed into copper(I)-promoted conjugate addition,[16] attention was turned to [(*E*)-2-(trimethylsilyl)vinyl]lithium.[17] When the reactant and this reagent were brought together with cuprous iodide in ether solution at −78 °C, β-keto ester **12** was obtained in 53% yield. Further definition of the dolastane A-ring substitution pattern was smoothly achieved by condensation of the enolate anion of **12** with diethyl phosphorochloridate and coupling of the enol phosphate with lithium dimethylcuprate.[18]

Chemical modification of the vinylsilane moiety was the next order of business.[19,20] Admixture of equimolar amounts of **14** and *m*-chloroperoxybenzoic acid in $CDCl_3$ solution at 25 °C and monitoring of the progress of reaction



12 **13** **14** **15** **16**

by ^1H NMR revealed formation of a complex mixture of products. However, if the epoxidation was arrested after approximately 50% consumption of the vinyl silane and the chromatographically sensitive **15** was directly exposed to boron trifluoride etherate in wet methanol, the desired dimethyl acetal could be isolated in 20% yield.

Because of the inefficiency of this step, an alternative means for obtaining **17** was sought. Indeed, keto ester **17** could be produced in excellent (88%) yield by copper-mediated addition of allylmagnesium bromide to **8**. Its subsequent conversion to **19** was virtually as successful. The unsaturated sidechain in **19** was next selectively cleaved by exposure to low concentrations of ozone at −78 °C in methanol–dichloromethane solution[21] until the

(4) Marshall, J. A.; Cohen, N.; Hochstetler, A. R. *J. Am. Chem. Soc.* **1966**, *88*, 3408.

(5) Although **6** has previously been described [Nazarov, I. N.; Zav'ialov, S. I. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1959**, 639], we have not been able to repeat this work satisfactorily.

(6) Direct access to **6** by the usual protocol involving bromination–dehydrobromination (a tertiary amine) of 3-methyl-2-cyclohexenone was also not feasible because of its marked propensity to aromatize under the mildest alkaline conditions.

(7) (a) Manning, M. J.; Raynolds, P. W.; Swenton, J. S. *J. Am. Chem. Soc.* **1976**, *98*, 5008. (b) Swenton, J. S.; Jackson, D. K.; Manning, M. J.; Raynolds, P. W. *Ibid.* **1978**, *100*, 6182. (c) Jackson, D. K.; Narasimhan, L.; Swenton, J. S. *Ibid.* **1979**, *101*, 3898. (d) Swenton, J. S.; Anderson, D. K.; Jackson, D. K.; Narasimhan, L. *J. Org. Chem.* **1981**, *46*, 4825. (e) Shih, C.; Fritzen, E. L.; Swenton, J. S. *Ibid.* **1980**, *45*, 4462. (f) Shih, C.; Swenton, J. S. *Ibid.* **1982**, *47*, 2825.

(8) House, H. O.; McDaniel, W. C. *J. Org. Chem.* **1977**, *42*, 2155.

(9) (a) Branca, S. J.; Smith, A. B., III. *J. Am. Chem. Soc.* **1978**, *100*, 7767. (b) Guaciaro, M. A.; Wookulich, P. M.; Smith, A. B., III. *Tetrahedron Lett.* **1978**, 4661. (c) Smith, A. B., III.; Branca, S. J.; Pilla, N. N.; Guaciaro, M. A. *J. Org. Chem.* **1982**, *47*, 1855.

(10) (a) Salomon, R. G.; Salomon, M. F. *J. Org. Chem.* **1975**, *40*, 1488. (b) Torn, T.; Kurozumi, S.; Tanaka, T.; Miura, S. *Tetrahedron Lett.* **1976**, 4087. (c) Jackson, W. P.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1516.

(11) A comparable synthon in the cyclopentene series has proven synthetically useful [ref 9b; Janssen, C. G. M.; Simons, L. H. J. G.; Godefroi, E. F. *Synthesis* **1982**, 389]. The difference in reactivity is noteworthy.

(12) Shiroyan, F. R.; Khazhakyan, L. V.; Mkrtchyan, A. R.; Terzyan, A. G.; Tatevsyan, G. T. *Arm. Khim. Zh.* **1967**, *20*, 649; *Chem. Abstr.* **1968**, *69*, 10387v.

(13) Rathke, M. W.; Lindert, A. *J. Am. Chem. Soc.* **1971**, *93*, 2318.

(14) An allied observation has been made in a different context: Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.

(15) Lau, K. S. Y.; Schlosser, M. *J. Org. Chem.* **1978**, *43*, 1595.

(16) This organolithium reagent was prepared by metal–halogen exchange of the (*Z*)-bromide with *tert*-butyllithium and by metal–metal exchange of the (*Z*)-tri-*n*-butylstannane derivative with *n*-butyllithium. Catalysis of the conjugate addition by CuI and $CuBr{\cdot}SMe_2$ in ether and tetrahydrofuran solvents was given particular attention.

(17) Boeckman, R. K., Jr.; Bruza, K. J. *J. Org. Chem.* **1979**, *44*, 4781.

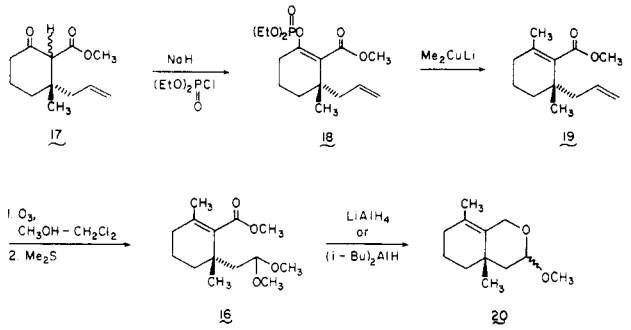
(18) (a) Sum, F.-W.; Weiler, L. *Can. J. Chem.* **1979**, *57*, 1431. (b) Sum, F. W.; Weiler, L. *Tetrahedron Suppl.* **1981**, *37*, 303.

(19) (a) Stork, G.; Colvin, E. *J. Am. Chem. Soc.* **1971**, *93*, 2080. (b) Stork, G.; Jung, M. E. *Ibid.* **1974**, *96*, 3682. (c) Stork, G.; Jung, M. E.; Colvin, E.; Noel, Y. *Ibid.* **1974**, *96*, 3684. (d) Paquette, L. A.; Han, Y.-K. *Ibid.* **1981**, *103*, 1831.

(20) (a) Bizant, V.; Matousek, V. *Collect. Czech. Chem. Commun.* **1958**, *24*, 3758. (b) Pleuddeman, E. P.; Fanger, G. *J. Am. Chem. Soc.* **1959**, *81*, 2632. (c) Sakurai, H.; Hayashi, N.; Kumada, M. *J. Organomet. Chem.* **1969**, *18*, 351. (d) Eisch, J. J.; Trainor, J. T. *J. Org. Chem.* **1963**, *28*, 487. (e) Fristad, W. E.; Bailey, T. R.; Paquette, L. A. *Ibid.* **1980**, *45*, 3028.

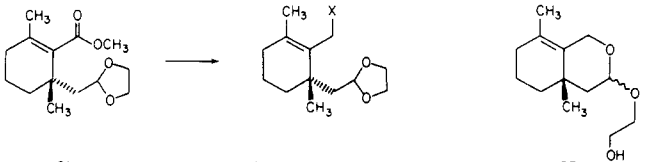
(21) (a) Heyl, F. W.; Herr, M. E. *J. Am. Chem. Soc.* **1950**, *72*, 2617. (b) Slomp, G.; Johnson, J. L.; *Ibid.* **1958**, *80*, 915. (c) Johnson, W. S.; Rubin, M. B. *Ibid.* **1963**, *85*, 1409. (d) Veysoglu, T.; Mitscher, L. A.; Swayse, J. K. *Synthesis* **1980**, 807.

starting material was just consumed (TLC analysis). By making recourse to reductive workup with dimethyl sulfide in this solvent system, there arose no need to isolate the aldehyde. Rather, in situ acetalization occurred to deliver **16** directly in 96% overall yield.



17 18 19 16 20

Interestingly, treatment of **16** with diisobutylaluminum hydride or lithium aluminum hydride resulted uniquely in formation of cyclic acetal **20**. This complication was easily bypassed by making recourse to **21** as an alternative starting material. In this instance, alcohol **22a** was obtained in 98% yield. No hint of cyclic acetate **23** was found, presumably because thermodynamics now favor **22a**.[22]



21 23

22a, X = OH **d**, X = SOPh
b, X = Cl **e**, X = SO_2Ph
c, X = SPh **f**, X = CN

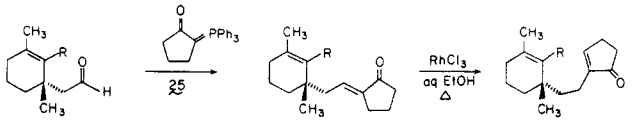
All attempts to transform **22a** into the allylic bromide by a myriad of methods failed. The problem appeared not be associated with production of the bromide but with its very high reactivity. It will be noted that the ether oxygens in **22** are six centers removed from the allylic carbon. These heteroatoms could serve to promote solvolysis of the halide via neighboring group participation. For this reason, recourse was made instead to the less reactive chloride **22b**.

The *N*-chlorosuccinimide–dimethyl sulfide complex acted on **22a** at 0 °C to deliver **22b** efficiently.[23] Although the chloride could be isolated in approximately 95% pure condition, it suffered extensive decomposition when chromatographed or allowed to stand at room temperature for several hours.

As expected, S_N2 displacement reactions on **22b** proceeded without competition from the S_N2' pathway. Sulfide **22c**, sulfone **22e**, and nitrile **22f** represent three end products of this chemistry. However, we were thwarted in our efforts to transform **22b** into a useful organometallic reagent and to induce the anions of sulfoxide **22d** and sulfone **22e** to undergo Michael condensation with 2-cyclopentenone.

While we had no success in attaching a five-membered ring to the activated methylene group in **22c–f**, the aldehydes derived from these acetals, viz., **24a–d**, underwent smooth condensation with (α-ketocyclopentylidene)triphenylphosphorane (**25**)[24] to furnish the highly functionalized α-methylenecyclopentanones **26**. Although **26a** suffered destruction when heated with rhodium trichloride in aqueous ethanol,[25] this reagent cleanly isomerized its congeners **26b–d** to the desired 2-cyclopentenones **27b–d**.

The above results set the stage for implementing intramolecular Michael condensations. As noted elsewhere by others, allylic sulfonyl carbanions enter readily into alkylation reactions with excellent α-regioselectivity.[26] These ambident anions are also recognized for their ability



24 25 26 27

a, R = CH_2SPh; **b**, R = CH_2SO_2Ph; **c**, R = CH_2CN; **d**, R = $COOCH_3$

to add 1,4-α to both acyclic and cyclic enones if hexamethylphosphoramide is present in the medium.[27] No previous example of an intramolecular variant of this process appears to have been documented. Where formation of a seven-membered ring is concerned, reasonable but not overwhelming levels of kinetic retardation can be expected. Nonetheless, prolonged stirring of the lithium, sodium, and potassium salts of **27b** in a range of nonpolar aprotic media did not result in cyclization. Of course, the possibility cannot be discounted that ring closure was operative and that the retro-Michael reaction was kinetically faster. Not surprisingly, the same fate awaited the cyano derivative **27c**.

Taken as a whole, the lack of success associated with the basic A + C → ABC strategy outlined in this report points up the possible inappropriateness of generating the dolastane framework by interior intramolecular cyclization. Alternative protocols that bypass all dependence on forming the cycloheptane ring in this manner need to be devised. Innovations of this type are currently under active investigation in these laboratories.

Experimental Section

2-Bromo-3-ethoxy-2-cyclohexenone (5). *N*-Bromosuccinimide (11.2 g, 63 mmol) was slowly added via a Gooch tube to a stirred solution of **4** (8.0 g, 57 mmol) in 100 mL of carbon tetrachloride at 0 °C in the dark. Upon completion of the addition, the mixture was stirred for 1 h at 0 °C and 1.5 h at 25 °C, at which point the solvent was removed in vacuo (25 °C). The residue was taken up in methylene chloride (60 mL), washed with ice-cold saturated aqueous sodium bicarbonate solution (2 × 50 mL) and ice water (2 × 25 mL), and dried. Removal of solvent under reduced pressure gave 11.2 g (90%) of **5** as a colorless solid, mp 85–87 °C (lit.[14] mp 87.5–90 °C): ^1H NMR (90 MHz, $CDCl_3$) δ 4.25 (q, J = 10 Hz, 2 H), 2.60 (m, 4 H), 2.05 (m, 2 H), 1.45 (t, J = 10 Hz, 3 H).

2-Bromo-3-methyl-2-cyclohexenone (6). Methyllithium (54.0 mL of 1.25 M in ether, 67.0 mmol) was slowly added via cannula to a stirred solution of **5** (1.33 g, 61 mmol) in 125 mL of dry tetrahydrofuran at 0 °C. The reaction mixture was stirred for 1 h at 0 °C and 1.5 h at 25 °C and quenched with 2 N hydrochloric acid (150 mL). The aqueous phase was separated and extracted with ether (2 × 50 mL), and the combined organic layers were

(22) Compare: Schmidlin, J.; Wettstein, A. *Helv. Chim. Acta* **1963**, *46*, 2799.
(23) Corey, E. J.; Kim, C. U.; Takeda, M. *Tetrahedron Lett.* **1972**, 4339.
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(26) See, for example: (a) Campbell, R. V. M.; Crombie, L.; Findley, D. A. R.; King, R. W.; Pattenden, G.; Whitting, D. A. *J. Chem. Soc., Perkin Trans 1* **1975**, 897. (b) Torii, S.; Uneyama, K.; Isihara, M. *Chem. Lett.* **1974**, 479. (c) Uneyama, K.; Torii, S. *Tetrahedron Lett.* **1976**, 443. (d) Torii, S.; Uneyama, K.; Kuyama, M. *Ibid.* **1976**, 1513. (e) Torii, S.; Uneyama, K.; Hamada, K. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2503. (f) Nokami, J.; Ono, T.; Kurihara, H.; Wakabayashi, S. *Chem. Lett.* **1982**, 607.
(27) (a) Hirama, M. *Tetrahedron Lett.* **1981**, 1905. (b) For cyanoethylation, see Sanchez, I. H.; Aguilar, M. A. *Synthesis* **1981**, 55.

washed with saturated aqueous sodium bicarbonate solution (50 mL) prior to drying. Removal of solvent under reduced pressure gave 8.27 g (72%) of **6**, which was used without further purification: IR (CCl_4, cm^{-1}) 2920 (s), 1695 (s), 1605 (s), 1255 (s); ^1H NMR (60 MHz, $CDCl_3$) δ 2.55 (m, 4 H), 2.20 (s, 3 H), 2.00 (m, 2 H).

Ketalization of 6. A stirred solution of **6** (4.34 g, 23 mmol), ethylene glycol (29 mL, 360 mmol), and *p*-toluenesulfonic acid monohydrate (100 mg, 0.5 mmol) in 250 mL of benzene was heated at reflux for 24 h under a Dean–Stark trap. The cooled reaction mixture was treated with saturated aqueous sodium bicarbonate solution (100 mL), and the aqueous phase was separated and extracted with ether (2 × 50 mL). The combined organic phases were washed with brine (100 mL) and dried. Removal of the solvent under reduced pressure gave 5.1 g (95%) of **7**: IR (CCl_4, cm^{-1}) 2960 (s), 2890 (s), 1445 (m), 1280 (s); ^1H NMR (90 MHz, $CDCl_3$) δ 4.10 (m, 2 H), 3.90 (m, 2 H), 2.10 (m, 2 H), 1.90 (s, 3 H), 1.75 (m, 4 H); MS, *m/z* calcd (M^+) 232.0099, obsd 232.0105.

2-Oxo-6-methyl-2,3-dihydropyran (10).[12] A solution of 4-acetylbutyric acid (15.0 g, 0.115 mol) in 300 mL of benzene was stirred as 10.92 mL (0.150 mol) of thionyl chloride was added. The solution was heated at reflux for 10 h, cooled, and freed of bulk solvent in vacuo. Distillation of the dark residue gave 12.0 g (80%) of **10** as a clear colorless oil, bp 100 °C (40 torr): IR (CCl_4, cm^{-1}) 2920 (w), 1780 (s), 1380 (m), 1240 (s); ^1H NMR (60 MHz, $CDCl_3$) δ 4.90 (m, 1 H), 2.60–1.90 (m, 4 H), 1.80 (d, J = 1 Hz, 3 H).

Methyl 3-Methyl-1-oxo-2-cyclohexene-2-carboxylate (8). Diisopropylamine (10.1 g, 0.10 mol) was added dropwise to a stirred solution of 68.5 mL (0.10 mol, 1.55 M) of *n*-butyllithium in 150 mL of dry tetrahydrofuran at −20 °C. The reaction mixture was cooled to −78 °C and 7.40 g (0.10 mol) of methyl acetate in 5 mL of tetrahydrofuran was added dropwise. After 0.5 h, 12.0 g (0.10 mol) of **10** dissolved in 10 mL of tetrahydrofuran was added in one portion. The solution was stirred at −78 °C for 4 h and at 25 °C for 8 h prior to quenching with 2 N hydrochloric acid (250 mL). The aqueous phase was separated and extracted with ether (2 × 100 mL). The combined organic phases were washed with saturated sodium bicarbonate solution (100 mL), dried ($MgSO_4$), and evaporated to leave a yellow oil. Fractional distillation through a 10-cm Vigreux column furnished 6.7 g (40%) of **8** as a pale yellow oil, bp 109–111 °C (0.9 torr): IR ($CDCl_3$, cm^{-1}) 1730 (s), 1670 (s); ^1H NMR (200 MHz, $CDCl_3$) δ 3.83 (s, 3 H), 2.54–2.37 (m, 6 H), 1.99 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 194.98, 167.31, 160.70, 133.08, 52.07, 36.96, 31.74, 22.15, 21.72; MS, *m/z* calcd (M^+) 168.0786, obsd 168.0790.

Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.45; H, 7.28.

Methyl 2-Methyl-6-oxo-2-[(*E*)-2-(trimethylsilyl)vinyl]-cyclohexanecarboxylate (12). *tert*-Butyllithium (9.6 mL, 18.8 mmol) in 50 mL of dry ether at −78 °C was treated dropwise with (*E*)-(2-bromovinyl)trimethylsilane (1.72 g, 9.4 mmol) in 3 mL of the same solvent. After being stirred at −20 °C for 1 h, the resulting solution was added slowly to a cold (−78 °C) stirred suspension of cuprous iodide (0.90 g, 4.7 mmol) in 1.25 mL of ether. The black mixture was stirred at −20 °C for 1 h and cooled to −78 °C, and **8** (0.80 g, 4.7 mmol) in 3 mL of ether was introduced in dropwise fashion. After 5 h at −78 °C, the reaction mixture was poured onto aqueous ammonium chloride/ammonium hydroxide solution (pH 8, 200 mL) and was allowed to stand for 12 h, at which point it was filtered through glass wool. The aqueous layer was extracted with ether (100 mL), and the combined organic phases were washed with dilute ammonium hydroxide (100 mL) and brine (100 mL) prior to drying. Removal of solvent and silica gel chromatography (elution with 10% ethyl acetate in hexane) afforded 0.73 g (53%) of **12** as a clear pale yellow oil: ^1H NMR (60 MHz, $CDCl_3$) δ 5.8 (m, 2 H), 3.8 and 3.75 (two s, total 3 H), 3.0–1.4 (br m, 7 H), 1.3 and 1.2 (two s, total 3 H), 0.20 (s, 9 H); MS, *m/z* calcd (M^+) 268.1495, obsd 268.1502.

1-Carbomethoxy-6-methyl-6-[(*E*)-2-(trimethylsilyl)-vinyl]-1-cyclohexen-2-yl Diethyl Phosphate (13). To a stirred suspension of sodium hydride (60 mg, 2.7 mmol) in 40 mL of dry ether was added **12** (0.73 g, 2.5 mmol) dissolved in 2 mL of ether. After 10 min of stirring, 0.44 g (2.5 mmol) of distilled diethyl phosphorochloridate in 2 mL of ether was introduced dropwise. The reaction mixture was stirred for 2 h, treated with excess solid ammonium chloride, and after 20 min, filtered through Celite. Removal of the solvent afforded 1.01 g (100%) of **13** as a clear colorless oil: IR ($CDCl_3$, cm^{-1}) 1720 (s), 1600 (m), 1430 (s), 1260 (s); ^1H NMR (60 MHz, $CDCl_3$) δ 6.17 (d, J = 18 Hz, 1 H), 5.78 (d, J = 18 Hz, 1 H), 4.25 (quintet, J = 9.5 Hz, 4 H), 3.70 (s, 3 H), 2.65–2.35 (m, 2 H), 1.90–1.30 (m, 13 H), 0.18 (s, 9 H); MS, *m/z* calcd (M^+) 404.1784, obsd 404.1793.

Methyl 2,6-Dimethyl-6-[(*E*)-2-(trimethylsilyl)vinyl]-1-cyclohexene-1-carboxylate (14). Methyllithium (1.8 mL, 2.25 mmol) was added dropwise to a stirred suspension of cuprous iodide (0.215 g, 1.13 mmol) in 25 mL of dry ether at −20 °C. To the resulting clear solution was added 0.23 g (0.56 mmol) of **13** dissolved in 4 mL of ether, and the reaction mixture was stirred for 3 h at −20 °C before being poured onto aqueous ammonium chloride/ammonium hydroxide solution (pH 8, 50 mL). The aqueous phase was separated and extracted with ether (25 mL). The organic phases were combined, washed with dilute ammonium hydroxide (25 mL) and brine (25 mL), and dried. Solvent evaporation afforded 0.12 g (81%) of **14** as a pale yellow oil: IR (CCl_4, cm^{-1}) 3010 (s), 2970 (s), 1723 (s), 1650 (w), 1608 (m), 1270 (s); ^1H NMR (200 MHz, $CDCl_3$) δ 5.95 (d, J = 19 Hz, 1 H), 5.60 (d, J = 19 Hz, 1 H), 3.63 (s, 3 H), 2.01 (m, 2 H), 1.71 (s, 3 H), 1.63–1.45 (m, 4 H), 1.20 (s, 3 H), 0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.46, 153.27, 136.81, 132.78, 126.86, 50.69, 41.17, 36.75, 31.36, 24.15, 21.51, 18.35, −1.12; MS, *m/z* calcd (M^+) 266.1702, obsd 266.1712.

Methyl 6-(2,2-Dimethoxymethyl)-2,6-dimethyl-1-cyclohexene-1-carboxylate (16). A stirred solution of **14** (0.400 g, 1.5 mmol) in 10 mL of methylene chloride was treated with 0.60 g (3.1 mmol) of 80% *m*-chloroperoxybenzoic acid. After 20 min, methylene chloride (20 mL) and 5% aqueous sodium hydroxide solution (30 mL) were added, and the organic phase was separated and dried. Solvent evaporation afforded a 1:1 mixture of **19** and **20** (^1H NMR analysis). A portion of this mixture (0.20 g, 0.35 mmol of **20**) was dissolved in 8 mL of methanol containing two drops of water, and boron trifluoride etherate (0.10 g, 0.7 mmol) was introduced at 25 °C. The reaction mixture was stirred for 2 h, at which point ether (10 mL) and saturated aqueous sodium bicarbonate solution (15 mL) were added. After 1 h, the organic phase was washed with brine (10 mL), dried, and freed of solvent. The oily mixture of products was subjected to Florisil chromatography (elution with 10% ethyl acetate/petroleum ether), and 20 mg (20%) of **16** was isolated: IR (CCl_4, cm^{-1}) 2980 (s), 2930 (s), 1725 (s), 1270 (s); ^1H NMR (200 MHz, $CDCl_3$) δ 4.45 (d, J = 4.4 Hz, 1 H), 4.42 (d, J = 4.8 Hz, 1H), 3.73 (s, 3 H), 3.28 (s, 6 H), 2.00 (m, 2 H), 1.78 (m, 2 H), 1.68 (s, 3 H), 1.65 (m, 2 H), 1.25 (m, 2 H), 1.14 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.80, 136.08, 134.58, 102.78, 52.48, 52.14, 50.98, 42.19, 35.05, 34.57, 31.36, 26.70, 21.65, 13.45; MS, *m/z* calcd (M^+) 256.1674, obsd 256.1668.

Methyl 2-Allyl-2-methyl-6-oxocyclohexanecarboxylate (17). To a stirred suspension of cuprous iodide (5.44 g, 28.6 mmol) in 125 mL of dry tetrahydrofuran at −78 °C was added 28.5 mmol of allylmagnesium bromide dissolved in ether. The reaction mixture was maintained at −20 °C until a muddy green color developed and then immediately returned to −78 °C. Keto ester **8** (4.0 g, 23.8 mmol) in 10 mL of tetrahydrofuran was introduced dropwise. After 1 h, the suspension was diluted with ether (100 mL) and aqueous ammonium chloride/ammonium hydroxide solution (pH 8, 150 mL) was added. The phases separated and the aqueous layer was extracted with ether (100 mL). The combined organic solutions were washed with saturated ammonium chloride solution (50 mL) and brine (50 mL) prior to drying and solvent evaporation. Distillation in a Kugelrohr apparatus delivered **17** (4.38 g, 88%) as a clear colorless oil (bp 100–115 °C (0.2 torr)): IR ($CDCl_3$, cm^{-1}) 2930 (s), 1710 (s), 1625 (s), 1435 (s), 1220 (s); ^1H NMR (200 MHz, $CDCl_3$) δ 5.60 (m, 1 H), 4.94 (m, 2 H), 3.53 (s, 3 H), 3.14 and 3.05 (two s, total 1 H), 2.55 (m, 1 H), 2.25 (m, 1 H), 1.95–1.45 (m, 6 H), 0.92 and 0.81 (two s, total 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 206.70, 206.52, 169.19, 133.27, 133.02, 119.07, 118.46, 67.18, 65.60, 51.70, 44.60, 42.54, 41.63, 41.51, 39.70, 39.20, 34.04, 32.65, 24.15, 22.21, 21.48; MS, *m/z* calcd (M^+) 210.1256, obsd 210.1263.

1-Carbomethoxy-6-allyl-6-methyl-1-cyclohexenyl Diethyl Phosphate (18). To a stirred suspension of sodium hydride (0.14 g, 5.83 mmol) in 40 mL of dry ether was added a solution of **17** (1.10 g, 5.25 mmol) in 10 mL of ether. After 10 min, distilled

diethyl phosphorochloridate (0.99 g, 5.74 mmol) in 10 mL of ether was introduced dropwise and followed 2 h later with saturated aqueous ammonium chloride solution (50 mL). The phases were separated, and the organic layer was washed with saturated aqueous sodium bicarbonate solution (40 mL), dried, and evaporated. There was obtained 1.41 g (80%) of **18** as a yellow oil: ^{1}H NMR (60 MHz, $CDCl_3$) δ 6.20–5.50 (m, 1 H), 5.20 (s, 1 H), 5.10–4.90 (m, 1 H), 4.20 (quintet, J = 8 Hz, 4 H), 3.80 (s, 3 H), 2.60–2.30 (m, 4 H), 1.40 (t, J = 8 Hz, 6 H), 1.90–1.30 (m, 4 H), 1.20 (s, 3 H).

Methyl 6-Allyl-2,6-dimethyl-1-cyclohexene-1-carboxylate (19). Methyllithium (14.1 mL, 17.6 mmol) was added dropwise to a stirred suspension of cuprous iodide (1.68 g, 8.0 mmol) in 50 mL of dry ether at −20 °C. The resulting clear solution was treated with **18** (1.40 g, 4.0 mmol) dissolved in 8 mL of ether and stirred for 4 h, at which time it was poured onto aqueous ammonium chloride/ammonium hydroxide solution (pH 8, 75 mL). The aqueous phase was separated and extracted with ether (50 mL), and the combined organic layers were washed with saturated ammonium chloride solution (25 mL) and brine (25 mL), dried, and evaporated. Distillation in a Kugelrohr apparatus afforded 0.56 g (67%) of **19** as a clear colorless oil (bp 95–110 °C (0.2 mm)); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.80 (m, 1 H), 5.00 (m, 2 H), 3.74 (s, 3 H), 2.24 (m, 2 H), 1.99 (m, 2 H), 1.68 (s, 3 H), 1.71–1.58 (m, 2 H), 1.30 (m, 2 H), 1.10 (s, 3 H); MS, m/z calcd (M^+) 208.1463, obsd 208.1469.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.05; H, 9.71.

Selective Ozonolysis of 19. A solution of **19** (0.50 g, 2.4 mmol) in 50 mL of dry methanol and 30 mL of methylene chloride was chilled to −78 °C in a 100-m*l* three-necked flask equipped with a magnetic stirrer, gas dispersion tube, and gas outlet. Ozone was bubbled through the solution in 100-s spurts until analytical TLC disclosed the complete disappearance of **19**. Following purging of the solution with nitrogen, 5 mol of dimethylsulfide was added, and stirring was maintained for 3 h at −78 °C and for 9 h at 25 °C. The bulk solvent was removed under reduced pressure and the residue was partitioned between ether (100 mL) and water (50 mL). The ethereal layer was washed with brine (50 mL), dried, and concentrated to leave 0.58 g (95%) of **16** as a colorless oil having spectral properties identical with the acetal described earlier.

4a,5,6,7-Tetrahydro-3-methoxy-4a,8-dimethylisochroman (20). To a stirred solution of **16** (0.10 g, 0.39 mmol) in 15 mL of dry ether at −78 °C was added 1.56 mL (1.17 mmol) of diisobutylaluminum hydride. After 3 h, the reaction mixture was warmed to −20 °C, quenched with saturated aqueous ammonium chloride solution, and filtered. The organic phase was dried and concentrated to give 69 mg (90%) of **20** as a mixture of diastereomers. The isomers were separated by chromatography (MPLC, silica gel, elution with 15% ethyl acetate in hexane). The major component exhibited the following ^{1}H NMR spectrum: (200 MHz, $CDCl_3$) δ 4.60 (m, 1 H), 4.11 (m, 2 H), 3.27 (s, 3 H), 1.95 (m, 2 H), 1.65 (s, 3 H), 1.70–1.35 (m, 6 H), 1.22 (s, 3 H). The ^{13}C NMR spectrum of the mixture was also recorded: (75 MHz, $CDCl_3$) ppm 131.18, 130.79, 127.64, 126.76, 99.87, 99.33, 61.61, 56.07, 55.73, 55.01, 45.93, 45.20, 39.06, 39.03, 33.30, 32.62, 32.48, 32.24, 26.65, 25.20, 18.74, 18.50, 18.35, 18.21; MS, m/z calcd (M^+) 196.1463, obsd 196.1468.

Methyl 6-[(1,3-Dioxolan-2-yl)methyl]-2,6-dimethyl-1-cyclohexene-1-carboxylate (21). Ozone was bubbled through a stirred solution of **19** (2.0 g, 9.6 mmol) in 100 mL of methanol and 100 mL of methylene chloride at −78 °C until no **19** remained (TLC analysis). The solution was purged with nitrogen, 2.0 mL (30 mmol) of dimethyl sulfide was added, and the reaction mixture was allowed to warm to 25 °C overnight. The solvents were removed in vacuo and the residue was taken up in ether (200 mL), washed with water (100 mL) and brine (100 mL), and dried. The ether was evaporated and the oil was dissolved in benzene (150 mL). *p*-Toluenesulfonic acid (500 mg, 2.60 mmol) and ethylene glycol (6.0 g, 96.0 mmol) were added. The reaction mixture was heated at reflux under a Dean–Stark trap for 6 h, cooled, washed with saturated aqueous sodium bicarbonate solution (100 mL) and brine (100 mL), and dried. Removal of solvent afforded 2.0 g (82%) of **21** as a brown oil. Purification by silica gel chromatography (elution with 15% ethyl acetate in hexane) returned 1.82 g (75%) of **26** as a faint yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.84 (dd, J = 5.1 and 4.1 Hz, 1 H), 3.91–3.71 (m, 4 H), 3.69 (s, 3 H), 1.96–1.66 (m, 6 H), 1.63 (s, 3 H), 1.60–1.20 (m, 2 H), 1.13 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.79, 136.02, 134.44, 103.06, 64.73, 64.40, 51.12, 43.85, 34.88, 34.72, 31.27, 26.73, 21.65, 18.42; MS, m/z calcd (M^+ 254.1518, obsd 254.1525.

2-[[2-(Hydroxymethyl)-1,3-dimethyl-2-cyclohexen-1-yl]methyl]-1,3-dioxolane (22a). To a stirred suspension of lithium aluminum hydride (0.82 g, 22 mmol) in 125 mL of dry ether at 25 °C was added dropwise 1.82 g (7.2 mmol) of **21** dissolved in 25 mL of ether. After 2 h, the reaction mixture was quenched with saturated aqueous sodium sulfate solution, stirred for 0.5 h, and filtered. Drying the filtrate and solvent evaporation provided 1.59 g (98%) of **22a** as a clear colorless oil: IR (CCl_4, cm^{-1}) 3500 (m), 2940 (s), 1135 (s); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.79 (dd, J = 5.6 and 3.4 Hz, 1 H), 4.02 (d, J = 2.3 Hz, 2 H), 3.90–3.72 (m, 4 H), 1.60 (s, 1 H), 1.95 (m, 4 H), 1.72–1.20 (m, 4 H), 1.61 (s, 3 H), 0.971 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 135.74, 135.54, 103.02, 64.61, 64.52, 58.35, 44.37, 35.92, 32.62, 28.01, 19.95, 19.17.

2-[[2-(Chloromethyl)-1,3-dimethyl-2-cyclohexen-1-yl]methyl]-1,3-dioxolane (22b). To a stirred solution of *N*-chlorosuccinimide (0.32 g, 2.4 mmol) in 15 mL of methylene chloride at 0 °C was added 0.17 (2.7 mmol) of dimethyl sulfide. The suspension was chilled to −20 °C and 0.50 g (2.2 mmol) of **22a** dissolved in 4 mL of methylene chloride was added dropwise over 5 min. After 1 h at 0 °C, the solvent was removed in vacuo at 25 °C and the residue was dissolved in ether (150 mL). This solution was washed with water (20 mL) and brine (20 mL), dried, and evaporated at 25 °C. There was obtained 0.53 g (100%) of **22b** as a yellow oil that proved unstable to purification: ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.80 (t, J = 4.6 Hz, 1 H), 4.16 (d, J = 11.7 Hz, 1 H), 4.11 (d, J = 11.7 Hz, 1 H), 3.92–3.68 (m, 4 H), 2.03–1.20 (m, 8 H), 1.76 (s, 3 H), 1.13 (s, 3 H).

2-[2-[1,3-Dimethyl-2-[(phenylthio)methyl]-2-cyclohexen-1-yl]methyl]-1,3-dioxolane (22c). To a stirred suspension of lithium hydride (25 mg, 3.14 mmol) in 50 mL of dry tetrahydrofuran at 25 °C was added 0.346 g (3.14 mmol) of thiophenol in 10 mL of the same solvent. After 30 min, **22b** (0.700 g, 2.86 mmol) dissolved in 15 mL of tetrahydrofuran was added dropwise and stirring was maintained for 12 h. The reaction mixture was diluted with water and ether, washed with 10% aqueous sodium hydroxide solution (30 mL) and brine (50 mL), and dried. Solvent evaporation afforded 0.85 g (93%) of **27c** as a yellow oil. Purification by MPLC on silica gel (elution with 15% ethyl acetate in petroleum ether) returned 0.71 g (78%) of **22c** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.25 (m, 5 H), 4.83 (t, J = 4.7 Hz, 1 H), 3.94–3.77 (m, 4 H), 3.67 (d, J = 11.3 Hz, 1 H), 3.57 (d, J = 11.3 Hz, 1 H), 1.90 (m, 4 H), 1.78 (s, 3 H), 1.55 (m, 4 H), 1.17 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 138.97, 135.09, 131.26, 128.75, 128.47, 125.41, 103.11, 64.56, 64.45, 43.79, 36.46, 36.02, 32.80, 26.84, 20.55, 18.80; MS, m/z calcd (M^+) 318.1653, obsd 318.1662.

2-[2-[1,3-Dimethyl-2-[(phenylsulfinyl)methyl]-2-cyclohexen-1-yl]methyl]-1,3-dioxolane (22d). To a stirred solution of **22c** (0.100 g, 0.314 mmol) in 10 mL of methylene chloride at −78 °C was added dropwise 0.54 g (0.314 mmol) of 100% *m*-chloroperoxybenzoic acid dissolved in 5 mL of methylene chloride. After being stirred for 2 h at −78 °C, the reaction mixture was warmed *slowly* to 25 °C, diluted with methylene chloride (20 mL), washed with saturated aqueous sodium bicarbonate solution (2 × 20 mL) and brine (20 mL), and dried. Removal of the solvent gave 0.101 g (96%) of **22d** as an oily mixture of diastereomers: ^{1}H NMR (60 MHz, $CDCl_3$) δ 7.35 (m, 5 H), 4.80 (m, 1 H), 3.90 (m, 6 H), 2.20–1.20 (m, 14 H).

2-[2-[1,3-Dimethyl-2-[(phenylsulfonyl)methyl]-2-cyclohexen-1-yl]methyl]-1,3-dioxolane (22e). To a stirred solution of sodium benzenesulfinate (9.84 g, 0.06 mol) in 250 mL of freshly distilled dimethyl sulfoxide was added 7.42 g (0.03 mol) of **22b** in 25 mL of the same solvent. The reaction mixture was stirred at room temperature for 24 h, diluted with ether (400 mL), washed with water (100 mL) and brine (3 × 100 mL), dried, and evaporated. The resulting golden oil was purified by MPLC on silica gel (elution with 25% ethyl acetate in petroleum ether) to give 4.15 g (40% from **22a**) of **22e** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.84 (m, 2 H), 7.51 (m, 3 H), 4.63 (t, J = 4.5 Hz, 1 H), 3.95 (m, 2 H), 3.78 (m, 2 H), 3.63 (m, 2 H), 1.97 (m, 2 H),

1.68 (m, 4 H), 1.61 (s, 3 H), 1.55 (m, 2 H), 1.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 141.93, 140.95, 133.29, 129.19, 127.87, 125.04, 102.78, 64.57, 57.90, 44.18, 36.25, 33.35, 27.17, 22.20, 18.59; fragmentation at 70 eV prevented mass measurement of the molecular ion.

Anal. Calcd for $C_{19}H_{26}SO_4$: C, 65.11; H, 7.48. Found: C, 64.93; H, 7.59.

2-[[2-(Cyanomethyl)-1,3-dimethyl-2-cyclohexen-1-yl]-methyl]-1,3-dioxolane (22f). To a stirred solution of **22b** (0.200 g, 0.82 mmol) in 10 mL of dimethyl sulfoxide was added 0.11 g (1.64 mmol) of potassium cyanide. After being stirred at room temperature for 48 h, the reaction mixture was poured onto brine (40 mL) and the aqueous phase was extracted with ether (5 × 15 mL). The combined ethereal layers were washed with water (10 mL) and brine (30 mL), dried, and evaporated. The residual yellow oil was chromatographed on silica gel (elution with 15% ethyl acetate in petroleum ether) to give 0.10 g (52%) of **22f** as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.76 (t, J = 4.58 Hz, 1 H), 3.92 (m, 2 H), 3.78 (m, 2 H), 3.05 (d, J = 17.7 Hz, 1 H), 2.95 (d, J = 17.7 Hz, 1 H), 2.00 (m, 2 H), 1.84–1.50 (m, 4 H), 1.73 (s, 3 H), 1.45 (m, 2 H), 1.12 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 135.10, 126.62, 118.97, 102.57, 64.62, 43.46, 36.69, 35.97, 32.64, 26.41, 20.34, 18.75, 16.35; MS, m/z calcd (M^+) 235.1532, obsd 235.1545.

2-[2-[1,3-Dimethyl-2-[(phenylthio)methyl]-2-cyclohexen-1-yl]acetaldehyde (24a). A solution of **22c** (0.100 g, 0.314 mmol) and pyridinium tosylate (22 mg, 0.09 mmol) in 10 mL of acetone–water (10:1) was heated at reflux for 36 h. The cooled reaction mixture was diluted with ether (30 mL), washed with water (20 mL) and brine (20 mL), dried, and evaporated. There was isolated 71 mg (87%) of **24a** as a pale yellow oil: IR (neat, cm^{-1}) 2940 (s), 1740 (s), 1590 (w), 1483 (m), 1440 (m); ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.72 (t, J = 5 Hz, 1 H), 7.90 (m, 5 H), 4.03 (d, J = 13.0 Hz, 1 H), 3.93 (d, J = 13.0 Hz, 1 H), 2.75 (m, 2 H), 2.20 (m, 2 H), 1.90 (s, 3 H), 1.75 (m, 4 H), 1.20 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.60, 138.24, 136.42, 129.62, 128.95, 128.71, 125.86, 53.16, 37.56, 36.83, 33.01, 32.64, 27.24, 20.57, 18.81.

Comparable treatment of **22e** (2.0 g, 5.70 mmol) gave 1.58 g (90%) of **24b** as a pale yellow oil: ^{1}H NMR (60 MHz, $CDCl_3$) δ 9.80 (t, J = 3.0 Hz, 1 H), 7.90 (m, 2 H), 7.60 (m, 3 H), 4.05 (m, 2 H), 2.60 (d, J = 3.0 Hz, 2 H), 2.30–1.50 (m, 4 H), 1.75 (s, 3 H), 1.40–1.00 (m, 2 H), 1.25 (s, 3 H).

From analogous hydrolysis of **22f** (0.10 g, 0.424 mmol), there was recovered 80 mg (99%) of **24c**: ^{1}H NMR (60 MHz, $CDCl_3$) δ 10.0 (t, J = 3.0 Hz, 1 H), 3.20 (m, 2 H), 2.50 (m, 2 H), 2.30–1.50 (m, 6 H), 1.90 (s, 3 H), 1.30 (s, 3 H).

Hydrolysis of **21** (0.22 g, 0.87 mmol) in the predescribed manner gave 0.18 g (98%) of **24d**: IR ($CDCl_3$, cm^{-1}) 2940 (s), 2740 (w), 1715 (s), 1435 (m); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.69 (dd, J = 3.4 and 2.2 Hz, 1 H), 3.68 (s, 3 H), 2.54 (dd, J = 13.8 and 2.2 Hz, 1 H), 2.37 (dd, J = 13.8 and 3.4 Hz, 1 H), 1.97 (m, 2 H), 1.68 (s, 3 H), 1.63 (m, 4 H), 1.16 (s, 3 H).

Condensations of 24 with 25. General Procedure. A solution of **24a** (1.10 g, 4.0 mmol) and **25** (1.52 g, 4.42 mmol) in 50 mL of benzene was heated at reflux for 24 h. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (elution with 20% ethyl acetate in petroleum ether) to give 0.75 g (55%) of **26a** as a colorless oil: IR ($CDCl_3$, cm^{-1}) 2940 (s), 1718 (s), 1648 (s), 1590 (w), 1484 (m), 1443 (m); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.25 (m, 5 H), 6.56 (m, 1 H), 3.67 (d, J = 11.2 Hz, 1 H), 3.58 (d, J = 11.2 Hz, 1 H), 2.60 (d, J = 6.1 Hz, 1 H), 2.56 (d, J = 5.5 Hz, 1 H), 2.34 (m, 4 H), 1.95 (m, 4 H), 1.78 (s, 3 H), 1.56 (m, 4 H), 1.15 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 206.72, 138.75, 135.75, 133.51, 130.89, 128.91, 128.47, 125.59, 40.56, 38.90, 38.71, 36.16, 32.83, 27.21, 26.58, 20.57, 19.80, 18.97; MS, m/z calcd (M^+) 340.1861, obsd 340.1847.

For 26b. Aldehyde **24b** (1.38 g, 4.5 mmol) was condensed with 1.86 g (5.4 mmol) of ketophosphorane **25** to give 0.98 g (59%) of **26b** as a colorless oil: ^{1}H NMR (60 MHz, $CDCl_3$) δ 7.90 (m, 2 H), 7.60 (m, 3 H), 6.50 (m, 1 H), 4.00 (m, 2 H), 2.80–2.00 (m, 8 H), 2.0–0.90 (m, 6 H), 1.70 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 206.31, 141.31, 138.88, 133.20, 132.10, 129.05, 127.45, 124.70, 57.31, 39.87, 38.34, 38.08, 36.65, 32.91, 26.90, 26.26, 21.66, 19.49, 18.28, 13.93.

For 26b. Aldehyde **24c** (81 mg, 0.424 mmol) was condensed with 175 mg (0.51 mmol) of **25** to give 90 mg (83%) of **26c** as a pale yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.47 (m, 1 H), 3.05 (d, J = 17.7 Hz, 1 H), 2.94 (d, J = 17.7 Hz, 1 H), 2.60 (m, 2 H), 2.33 (m, 4 H), 2.00 (m, 4 H), 1.75 (s, 3 H), 1.59 (m, 4 H), 1.12 (s, 3 H).

For 26d. Aldehyde **24d** (0.80 g, 3.80 mmol) was condensed with 1.67 g (4.73 mmol) of **25** to give 0.79 g (73%) of **26d**: IR ($CDCl_3$, cm^{-1}) 2945 (s), 1720 (s), 1645 (s), 1435 (m), 1055 (s); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.57 (m, 1 H), 3.73 (s, 3 H), 2.57 (t, J = 4.94 Hz, 2 H), 2.34 (m, 4 H), 2.30 (m, 2 H), 1.94 (m, 2 H), 1.68 (s, 3 H), 1.62 (m, 4 H), 1.12 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 206.65, 170.75, 138.88, 136.64, 133.96, 132.93, 51.04, 40.37, 38.65, 37.05, 34.88, 31.30, 27.15, 26.25, 21.59, 19.80, 18.53; MS, m/z calcd ($M^+ - CH_3OH$) 244.1463, obsd 244.1427.

Rhodium Trichloride Promoted Isomerizations. General Procedure. To a solution of **26b** (0.20 g, 0.54 mmol) in 5 mL of ethanol was added 7.0 mg (0.03 mmol) of rhodium trichloride trihydrate in 0.5 mL of water, and the mixture was heated at reflux for 24 h. The cooled contents of the flask were poured onto ice water (10 mL) and extracted with ether (3 × 15 mL). The combined organic layers were washed with saturated sodium bicarbonate solution (30 mL) and brine (30 mL), dried, and evaporated to leave a yellow oil. Purification by silica gel chromatography (elution with 25% ethyl acetate in petroleum ether) gave 0.110 g (55%) of **27b** as a colorless oil: IR ($CDCl_3$, cm^{-1}) 2950 (s), 1700 (s), 1640 (w), 1450 (m), 1310 (s), 1150 (s); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.95 (m, 2 H), 7.60 (m, 3 H), 7.25 (m, 1 H), 4.15 (d, J = 12.5 Hz, 1 H), 4.05 (d, J = 12.5 Hz, 1 H), 2.50 (m, 2 H), 2.30 (m, 2 H), 2.10 (m, 4 H), 2.0–1.20 (m, 6 H), 1.65 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.91, 157.21, 146.61, 141.88, 140.92, 133.32, 129.23, 127.82, 125.21, 57.56, 38.14, 37.37, 35.07, 34.62, 33.41, 36.77, 27.51, 22.04, 19.61, 18.65.

Anal. Calcd for $C_{22}H_{28}SO_3$: C, 70.93; H, 7.58. Found: C, 70.60; H, 7.58.

For 27c. Isomerization of **26c** (90 mg, 0.35 mmol) in the above manner afforded 61 mg (68%) of **27c**, a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 1 H), 3.00 (d, J = 16.0 Hz, 1 H, 2.97 (d, J = 16.0 Hz, 1 H); 2.55 (m, 2 H), 2.38 (m, 2 H), 2.01 (m, 4 H), 1.74 (s, 3 H), 1.70–1.20 (m, 6 H), 1.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 209.78, 157.27, 146.41, 135.36, 126.61, 118.94, 38.07, 37.88, 34.62, 32.77, 29.70, 26.51, 26.00, 20.31, 19.93, 18.97, 15.84; MS, m/z calcd (M^+) 257.1780, obsd 257.1802.

For 27d. Isomerization of **26d** (790 mg, 2.86 mmol) in the predescribed fashion gave 602 mg (76%) of **27d** as a clear colorless oil: IR ($CDCl_3$, cm^{-1}) 2980 (w), 2940 (m), 2870 (w), 1705 (s), 1635 (w), 1435 (m), 1270 (m), 1230 (s), 1062 (s); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (m, 1 H), 3.70 (s, 3 H), 2.52 (m, 2 H), 2.36 (m, 2 H), 2.13 (m, 2 H), 1.64 (s, 3 H), 1.59 (m, 4 H), 1.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 209.78, 171.01, 156.95, 146.92, 135.87, 134.60, 51.04, 38.39, 36.28, 34.62, 33.92, 31.37, 26.45, 21.59, 19.61, 18.65 (one carbon not observed); MS, m/z calcd ($M^+ - CH_3OH$) 244.1463, obsd 244.1554.

Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.66; H, 8.87.

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Registry No. **4**, 5323-87-5; **5**, 51326-00-2; **6**, 51326-26-2; **7**, 98127-00-5; **8**, 86891-79-4; **9**, 3128-06-1; **10**, 3740-59-8; **12**, 98127-01-6; **13**, 98127-02-7; **14**, 98127-03-8; **16**, 98127-04-9; **17**, 98127-05-0; **18**, 98127-06-1; **19**, 98127-07-2; *cis*-**20**, 98127-08-3; *trans*-**20**, 98127-11-8; **21**, 98127-09-4; **22a**, 98127-10-7; **22b**, 98127-12-9; **22c**, 98127-13-0; **22d**, 98169-87-0; **22e**, 98127-14-1; **22f**, 98127-15-2; **24a**, 98127-16-3; **24b**, 98127-17-4; **24c**, 98127-18-5; **24d**, 98127-19-6; **25**, 2136-76-7; **26a**, 98127-20-9; **26b**, 98169-88-1; **26c**, 98127-21-0; **26d**, 98127-22-1; **27b**, 98127-23-2; **27c**, 98127-24-3; **27d**, 98127-25-4; (*E*)-BrCH=CHSiMe$_3$, 41309-43-7; H_2C=$CHCH_2Br$, 106-95-6; methyl acetate, 79-20-9; thiophenol, 108-98-5; sodium benzenesulfinate, 873-55-2.