d, $J$ = 9 Hz, aromatic next to carbonyl); IR (max) (KBr) 1715 (C=O), 3260 (O–H), 1270 (C–O), 1463 ($CH_2$–O), 1600, 1615 (d, C=C) $cm^{-1}$; $m/e$ (rel intensity) 150 (parent, 34), 149 (13), 121 (base peak, 100), 93 (21), 92 (14), 77 (12), 65 (43), 63 (28), 55 (19), 51 (17), 44 (43), 43 (22), 41 (25). Homophthalic anhydride: $^1$H NMR ($CDCl_3$) $\delta$ 4.12 (2 H, s, $CH_2$), 7.25–7.85 (3 H, m, aromatic), 8.10–8.25 (1 H, d with fine structure, $J$ = 8 Hz, aromatic next to carbonyl); IR (max) ($CHCl_3$) 1803, 1754 (d, C=O), 1605 (C=C), 1280 (C–O) $cm^{-1}$; $m/e$ 162.03168 (calcd for $C_9H_6O_3$, 162.03170). Methyl $N$-acetylanthranilate: $^1$H NMR ($CDCl_3$) $\delta$ 2.01 (3 H, s, $CH_3CO$), 3.80 (3 H, s, $CH_3O$–), 6.85–8.02 (3 H, m, aromatic), 8.55–8.70 (1 H, d with fine structure, $J$ = 14 Hz, aromatic next to carbonyl), 11.95 (1 H, br s, N–H); IR (max) ($CHCl_3$) 1705, 1685 (d, C=O), 1610, 1590 (d, C=C), 1265 (C–O), 3320 (N–H) $cm^{-1}$; $m/e$ 193.07491 (calcd for $C_{10}H_{11}NO_3$, 193.07390). Methyl 2-ureidobenzoate: $^1$H NMR ($CDCl_3$ + $Me_2SO$-$d_6$) $\delta$ 2.88 (2 H, s, $NH_2$), 3.90 (3 H, s, $CH_3$), 5.75 (1 H, br s, N–H), 6.95–8.05 (3 H, m, aromatic), 8.40–8.54 (1 H, d with fine structure, $J$ = 8 Hz, aromatic next to carbonyl); IR (max) (KBr) 1600, 1575 (d, C=C), 1260 (C–O), 3410 (N–H), 3270, 3210 (d, N–H) $cm^{-1}$; $m/e$ 194.06912 (calcd for $C_9H_{10}N_2O_3$, 194.06915).

**Acknowledgment.** The authors gratefully acknowledge the assistance of Drs. Bernhard Riefling and Hans-Hermann Lau and the generous support of the National Institutes of Health (GM24254). We also wish to recognize the National Science Foundation (CHE 76-80362) for funds used in the purchase of the Finnegan 4023 GC–mass spectrometer used in this work. Special thanks go to Johnson Matthey Inc. and Engelhard Industries for generous loans of palladium chloride used in this work.

**Registry No.** Benzene, 71-43-2; fluorobenzene, 462-06-6; methoxybenzene, 100-66-3; (1,1-dimethylethyl)benzene, 98-06-6; benzoic acid methyl ester, 93-58-3; 4-fluorobenzoic acid methyl ester, 403-33-8; 4-methoxybenzoic acid methyl ester, 121-98-2; 4-(1,1-dimethylethyl)-benzoic acid methyl ester, 26537-19-9; benzenemethanol, 100-51-6; 3-methoxybenzenemethanol, 6971-51-3; 3-hydroxybenzenemethanol, 620-24-6; 3-chlorobenzenemethanol, 873-63-2; 4-methylbenzenemethanol, 589-18-4; 2,5-dimethoxybenzenemethanol, 33524-31-1; 2,3-dimethoxybenzenemethanol, 5653-67-8; 1(3*H*)-isobenzofuranone, 87-41-2; 5-methoxy-1(3*H*)-isobenzofuranone, 4741-62-2; 5-hydroxy-1(3*H*)-isobenzofuranone, 55104-35-3; 5-chloro-1(3*H*)-isobenzofuranone, 54109-03-4; 6-methyl-1(3*H*)-isobenzofuranone, 72985-23-0; 4,7-dimethoxy-1-(3*H*)-isobenzofuranone, 64019-78-9; 4,5-dimethoxy-1(3*H*)-isobenzofuranone, 4741-58-6; benzeneethanol, 60-12-8; 3-methoxybenzeneethanol, 5020-41-7; $\alpha$-methylbenzeneethanol, 698-87-3; *trans*-2-phenylcyclohexanol, 2362-61-0; *cis*-2-phenylcyclohexanol, 16201-63-1; 1*H*-2-benzopyran-1-one, 491-31-6; 6-methoxy-1*H*-2-benzopyran-1-one, 20678-26-6; 3-methyl-1*H*-2-benzopyran-1-one, 29539-21-7; *trans*-1,2,3,4,4a,10b-hexahydro-6*H*-dibenzo[*b*,*d*]pyran-6-one, 72331-11-4; *cis*-1,2,3,4,4a,10b-hexahydro-6*H*-dibenzo[*b*,*d*]pyran-6-one, 72331-10-3; benzoic acid, 65-85-0; benzeneacetic acid, 103-82-2; benzenamide, 55-21-0; *N*-phenylacetamide, 103-84-4; phenylurea, 64-10-8; benzophenone, 119-61-9; 1,3-isobenzofurandione, 85-44-9; 1*H*-2-benzopyran-1,3(4*H*)-dione, 703-59-3; 1*H*-isoindole-1,3(2*H*)-dione, 85-41-6; 4-acetylaminobenzoic acid methyl ester, 17012-22-5; *N*-(2-methoxycarbonylphenyl)-urea, 2242-77-5; 2-benzoylbenzoic acid, 606-28-0; thallium(III) trifluoroacetate, 23586-53-0.

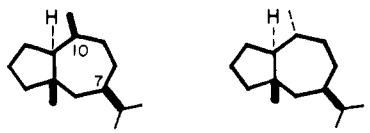
# Synthesis of Sesquiterpene Antitumor Lactones. 9.[1] The Hydronaphthalene Route to Pseudoguaianes. Total Synthesis of (±)-Confertin[†]

**Clayton H. Heathcock,* Eric G. DelMar, and Samuel Lindsay Graham**

*Contribution from the Department of Chemistry, University of California, Berkeley, California 94720.* *Received August 10, 1981*

**Abstract:** The feasibility of using hydronaphthalene precursors for the synthesis of pseudoguaianes has been examined. The dimethyldecalyl tosylate **13** was prepared as shown in Scheme II. Its solvolysis was studied in methanol and in buffered acetic acid. In methanol, **13** gives keto ether **14**, enone **15**, and cyclopropyl ketone **16**. In acetic acid, the products are **15** and **16**. In neither solvent is any hydroazulenone produced. The desoxy analogue **28** was prepared as shown in Scheme IV and solvolyzed in buffered acetic acid. The only products obtained are octalins **25** and **29**. The solvolytic behavior of tosylates **13** and **28** is compared with that of the related tosylates **17** and **21**, which had been studied earlier, and a mechanistic rationale is advanced to explain the divergent behavior. Vicinal diol monotosylate **34** has been prepared and solvolyzed in basic *tert*-butyl alcohol. The rearrangement of **34** can be made to give keto ester **35** by using lithium hydroxide or keto alcohols **36** and **37** by the use of potassium hydroxide. This novel difference in reaction course results from the fact that potassium hydroxide saponifies the transannular acetate group prior to solvolysis. The resulting diol tosylate adopts a different reacting conformation, leading to the production of **36** (Scheme VII). Keto ketal **39** is converted into enone **43** by a novel new reaction involving treatment of **39** sequentially with trimethylaluminum and methyllithium. Lithium/ammonia reduction of **43** gives hydroxy ketone **50**, which has been converted into (±)-helenalin. Catalytic hydrogenation of **43** gives **51**, which is converted via enol lactone **56** into acetoxy lactone **58**. This intermediate is converted by Danishefsky's procedure into (±)-confertin (**1**).

The pseudoguaianolides are a group of more than 100 sesquiterpenes having the general skeleton shown in i and ii. The family is subdivided into a more abundant group in which the $C_{10}$-methyl occupies the $\beta$-position on the *trans*-hydroazulene nucleus (the ambrosanolides, i) and a less abundant 10$\alpha$-configured group (the helenanolides, ii). Both subgroups have the $\beta$ configuration at $C_7$. Interest in the pseudoguaianolides has been strongly stimulated by the discovery that many members of the family have cytotoxic and antitumor properties[2] and chemists have reported total syntheses of 18 pseudoguaianolides since 1975.[3]




*i* *ii*

[†] Dedicated to Professor Gilbert Stork on the occasion of his 60th birthday.

(1) For part 8 see C. M. Tice and C. H. Heathcock, *J. Org. Chem.*, **46**, 9 (1981).

(2) S. M. Kupchan, M. A. Eakin, and A. M. Thomas, *J. Med. Chem.*, **14**, 1147 (1971).

(3) For a complete survey of the activity in this field see C. H. Heathcock, S. L. Graham, M. C. Pirrung, F. Plavac, and C. T. White in "The Total Synthesis of Natural Products", Vol. 5, J. W. ApSimon, Ed., Wiley, New York, 1982.

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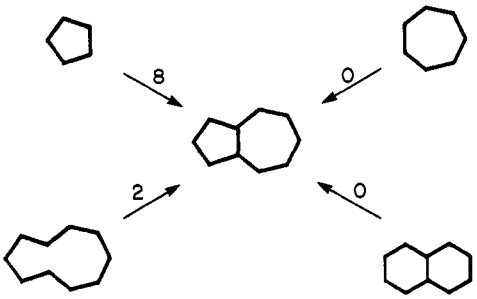
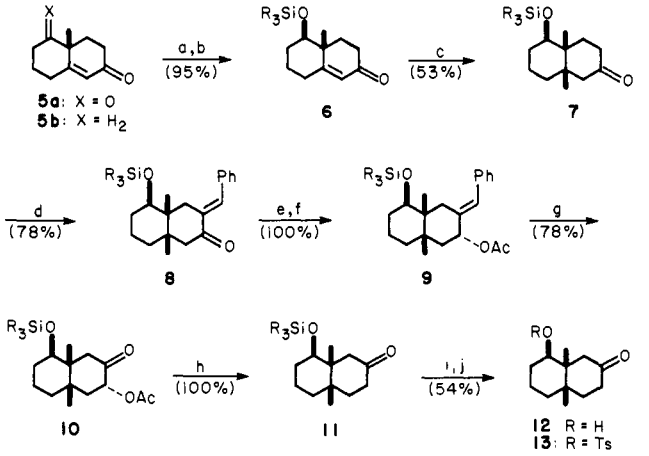
Scheme I




In devising syntheses of compounds such as i and ii, several broad strategies for construction of the hydroazulene skeleton come to mind. The first approach, and the one which has been employed in most of the successful syntheses which have been reported,[4-11] is to begin with a cyclopentane and then to add the cycloheptane ring. A complementary strategy would be to add the cyclopentane ring onto a preformed cycloheptane nucleus. No successful syntheses incorporating this strategy have been reported. A third approach, which has been employed in two syntheses,[12,13] is to form the hydroazulene skeleton by transannular cyclization of an appropriately constructed cyclodecane. Finally, it is possible to utilize a hydronaphthalene precursor, which is caused to undergo skeletal rearrangement to provide the desired hydroazulene skeleton. Although this approach has been useful for the synthesis of guaianes,[14] it has not been employed for total synthesis of naturally occurring pseudoguaianolides.[15] These basic strategies are summarized in Scheme I; the numbers on each arrow are the number of different synthetic approaches employing that strategy.

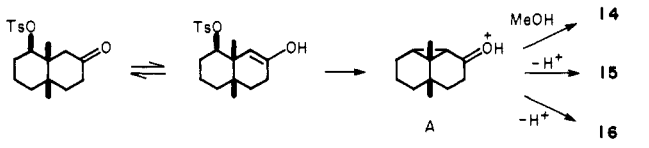
Since we had successfully employed the hydronaphthalene → hydroazulene route for synthesis of the guaianes bulnesol and bulnesene,[17] we have explored this strategy for synthesis of the pseudoguaiane skeleton. In this paper, we report the results of this investigation, which has resulted in a total synthesis of the ambrosanolide (±)-confertin (**1**) and a formal total synthesis of the helenanolide (±)-helenalin (**2**).

Scheme II

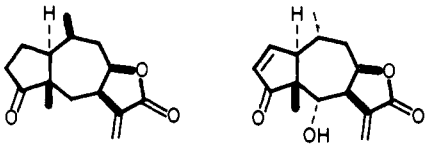



(a) $NaBH_4$, $i$-$C_3H_7OH$; (b) $t$-$BuMe_2SiCl$, imidazole; (c) $Me_2CuLi$; (d) benzaldehyde, NaOH, ethanol; (e) $NaBH_4$, methanol; (f) $Ac_2O$, pyridine; (g) $O_3$, EtOAc, methanol, hexane, −70 °C; (h) $Li/NH_3$; (i) HF, $H_2O$, THF, 25 °C; (j) $p$-TsCl, pyridine, 0 °C

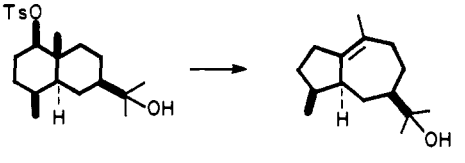
Scheme III




The key transformation in the aforementioned bulnesol synthesis was solvolytic rearrangement of decalyl tosylate **3** to the hydroazulene **4**.[17] With that precedent in mind, we prepared keto tosylate **13**, as shown in Scheme II. There were several noteworthy features of this synthesis. First, reaction of enone **6** with lithium dimethylcuprate gives a 60:40 mixture of the 1,4 adduct **7** and the corresponding 1,2 adduct. We have found competing 1,2 addition to be common in cuprate reactions on such octalones. The simple octalone **5b** reacts with lithium dimethylcuprate to give the 1,4 and 1,2 adducts in a ratio of 85:15.[18] A second noteworthy aspect of the sequence illustrated in Scheme II is the efficiency of the Meakins technique for 1,2-ketone transposition.[19] Although five steps are required, the transformation proceeds in quite acceptable overall yield (61%). Although Meakins found zinc/acetic acid to be a superior system for deacetylation of the

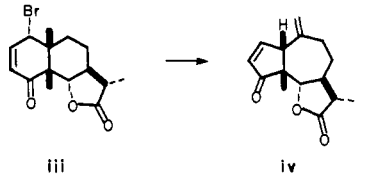



1 2




3 4

(4) J. A. Marshall and R. H. Ellison, *J. Am. Chem. Soc.*, **98**, 4312 (1976).
(5) (a) P. DeClercq and M. Vandewalle, *J. Org. Chem.*, **42**, 3447 (1977); (b) P. Kok, P. DeClercq, and M. Vandewalle, *Bull. Soc. Chim. Belg.*, **87**, 615 (1978); (c) *J. Org. Chem.*, **44**, 4553 (1979); (d) M. Demuynck, P. DeClercq, and M. Vandewalle, *ibid.*, **44**, 4863 (1979).
(6) (a) P. A. Grieco, Y. Ohfune, and G. Majetich, *J. Am. Chem. Soc.*, **99**, 7393 (1977); (b) P. A. Grieco, T. Oguri, S. Burke, E. Rodriguez, G. T. DeTitta, and S. Fortier, *J. Org. Chem.*, **43**, 4552 (1978); (c) Y. Ohfune, P. A. Grieco, C.-L. J. Wang, and G. Majetich, *J. Am. Chem. Soc.*, **100**, 5946 (1978); (d) P. A. Grieco, Y. Ohfune, and G. Majetich, *J. Org. Chem.*, **44**, 3092 (1979); (e) P. A. Grieco, Y. Ohfune, and G. Majetich, *Tetrahedron Lett.*, 3265 (1979).
(7) (a) P. T. Lansbury and A. K. Serelis, *Tetrahedron Lett.*, 1909 (1978); (b) P. T. Lansbury and D. Hangauer, *ibid.*, 3263 (1979); (c) P. T. Lansbury, D. Hanguaer, and J. P. Vacca, *J. Am. Chem. Soc.*, **102**, 3964 (1980).
(8) M. F. Semmelhack, A. Yamashita, J. C. Tomesch, and K. Hirotsu, *J. Am. Chem. Soc.*, **100**, 5565 (1978).
(9) P. A. Wender, M. A. Eissenstadt, and M. P. Filosa, *J. Am. Chem. Soc.*, **101**, 2196 (1979).
(10) (a) M. R. Roberts and R. H. Schlessinger, *J. Am. Chem. Soc.*, **101**, 7626 (1979); (b) G. J. Quallich and R. H. Schlessinger, *ibid.*, **101**, 7627 (1979).
(11) F. E. Ziegler and J.-M. Faug, *J. Org. Chem.*, **46**, 825 (1981).
(12) J. A. Marshall and W. R. Snyder, *J. Org. Chem.*, **40**, 1656 (1975).
(13) R. A. Kretchmer and W. S. Thompson, *J. Am. Chem. Soc.*, **98**, 3379 (1976).
(14) C. H. Heathcock in "The Total Synthesis of Natural Products", Vol. 2, J. W. ApSimon, Ed., Wiley, New York, 1973, pp 402–519.
(15) However, the first synthesis of the pseudoguaiane skeleton was Hendrickson's conversion of santonin into keto lactone iv by Wagner–Meerwein rearrangement of bromo octalone iii.[16]

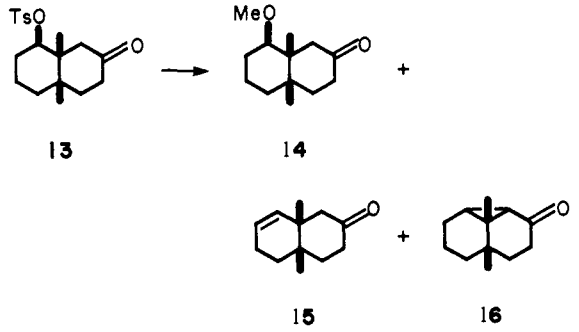



iii iv

(16) J. B. Hendrickson, C. Ganter, H. Link, and D. Dormass, *Tetrahedron Lett.*, 2235 (1968).
(17) C. H. Heathcock and R. Ratcliffe, *J. Am. Chem. Soc.*, **93**, 1746 (1971).
(18) Janice H. Johnson, M.S. Thesis, University of California, Berkeley, CA, 1976.
(19) J. E. Bridgeman, C. E. Butchers, E. R. H. Jones, A. Kasal, G. D. Meakins, and P. D. Woodgate, *J. Chem. Soc. C*, 244 (1970).

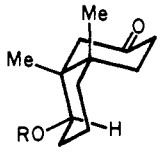
α-acetoxy ketone, compound **10** is recovered unchanged from such treatment. However, lithium/ammonia brings about the desired reduction in quantitative yield. Finally, we were unable to remove the *tert*-butyldimethylsilyl protecting group from **11** by either tetrabutylammonium fluoride or acetic acid in THF.[20] However, 3 M HF in aqueous THF smoothly converts keto ether **11** into keto alcohol **12**.

Solvolysis of keto tosylate **13** in refluxing methanol provides mainly methyl ether **14** (78%), accompanied by 7% of unsaturated ketone **15** and 10% of cyclopropyl ketone **16**. The stereostructure



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

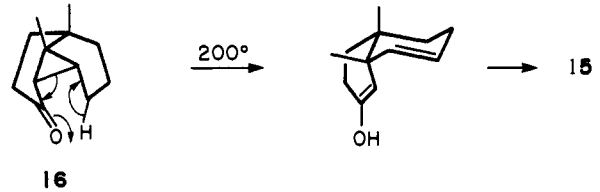
assigned to methyl ether **14** is based on its $^1$H NMR spectrum. The carbinol proton appears as a double doublet with $J$ = 11.0 and 4.1 Hz, at 2.96 ppm. This is a rather high-field resonance for such a proton. However, an upfield shift is expected for compound **14**, since the carbinol proton would lie over one face



**13**: R = Ts
**14**: R = Me

of the carbonyl group. A similar upfield shift is seen in the analogous resonance for tosylate **13**, which appears at 4.57 ppm, compared to 5.10 ppm for tosylate **28**. The products obtained from methanolysis of tosylate **13** might all arise from a bridged intermediate, as shown in Scheme III.

When the solvolysis of **13** is carried out at 100 °C in acetic acid buffered with potassium acetate, ketones **15** and **16** are the sole reaction products, in a 72:28 ratio. Control experiments show this to be the true kinetic product ratio under these conditions. That is, ketones **15** and **16** are found in the same 72:28 ratio after 2 h and 50 h reaction time. When keto tosylate **13** is treated with potassium *tert*-butoxide in refluxing *tert*-butyl alcohol, cyclopropyl ketone **16** and octalone **15** are obtained in a ratio of 97:3. Analysis of this mixture by GLPC is complicated by the fact that ketone **16** slowly rearranges to ketone **15** at 200 °C, presumably by the



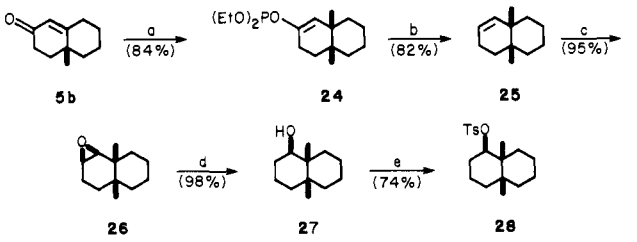
**16**

precedented[21] 1,5-hydrogen shift. The solvolysis products can again be explained with the aid of Scheme III, with the added proviso that acetic acid is not sufficiently nucleophilic to intercept the intermediate ion A. Under the buffered conditions of this experiment, ion A is diverted solely to products **15** and **16**.

The results obtained in solvolysis of keto tosylate **13** were disappointing, but not totally unexpected. For example, acetolysis

(20) E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, **94**, 6190 (1972).
(21) R. J. Ellis and H. M. Frey, *Proc. Chem. Soc.*, 221 (1964).

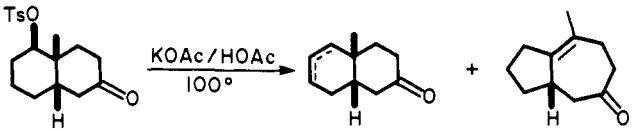
Scheme IV



**5b** **24** **25** **26** **27** **28**

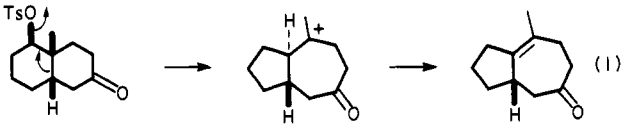
(a) (1) $Me_2CuLi$, ether, 0 °C; (2) $(EtO)_2POCl$, HMPT; (b) Li/$C_2H_5NH_2$, *tert*-butyl alcohol; (c) *m*-CPBA, $CHCl_3$, 25 °C; (d) $LiAlH_4$, ether; (e) *p*-TsCl, pyridine, 25 °C

of the related keto tosylate **17** gives only 9% of hydroazulenone **19**, the major product (87%) being a mixture of octalones (**18**).[22]



**17** **18** **19**

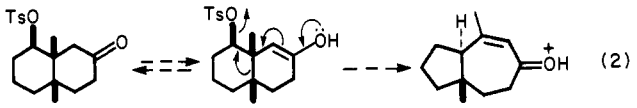
The poor yield of rearrangement product in this reaction was rationalized by the unfavorable electrostatic interaction resulting from bringing the cationic carbon one position nearer the positive end of the carbonyl dipole (eq 1). In the case of **13**, however,



(1)

**17** **19**

we had hoped that solvolysis might occur on the enolic form, which could rearrange directly to an oxonium ion (eq 2). The failure

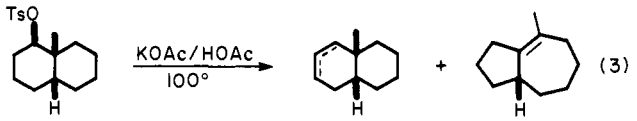


(2)

**13** **20**

of the plan put forth in eq 2 can readily be understood with the aid of molecular models. It is clear that, in the conformation of enol **20** having the tosylate group equatorial, the migrating bond and the enol double bond are nearly coplanar. That is, the migrating bond is approximately orthogonal to the π system of the enol. Thus, the developing carbocationic center cannot be delocalized by the enol.

In our earlier study, it was found that acetolysis of the desoxy analogue of **17** provides significantly more of the rearrangement product.[22] Thus, acetolysis of tosylate **21** gives octalins **22** and hydroazulene **22** in 42% and 54% yields, respectively (eq 3).

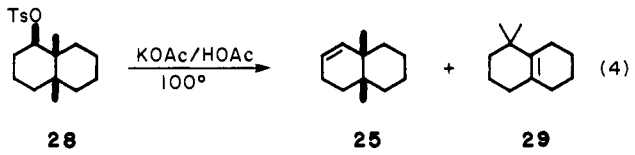


(3)

**21** **22** **23**

Therefore, we prepared the analogous tosylate **28** by the route shown in Scheme IV. The acetolysis of tosylate **28** was studied under conditions identical with those used for rearrangement of tosylate **21**. However, as shown in eq 4, no hydroazulene products are obtained. The major product is octalin **25** (75%) and the minor

(22) C. H. Heathcock, R. Ratcliffe, and J. Van, *J. Org. Chem.*, **37**, 1796 (1972).




28 25 29

product is rearranged alkene **29** (25%).

The acetolysis products from tosylates **21** and **28** may be rationalized by the mechanism outlined in Scheme V. If ionization occurs while the *cis*-decalin is in conformation A, the ring fusion bond is well disposed for migration and rearranged ion B can result.[22] When R = H, this mode of reaction represents 54% of the total reaction, but when R = Me, no product arises from this path. We postulate that the failure of tosylate **28** to give the rearranged ion B results from the increased torsional interactions which would be present in the transition state leading from A to B. That is, as the rearrangement commences, the two methyl groups, which bear a gauche relationship to one another in A, must be brought into an almost eclipsed relationship in the transition state. This increased steric interaction when R = Me raises the activation energy for rearrangement in that case.

If ionization occurs while the tosylate group is axial (conformation C), ion D may be formed and hence the simple elimination products **22** and **25**. This mode of reaction leads to 42% of the observed products from tosylate **21** and 70% from tosylate **28**. Conformation C can also lead to an immediate rearrangement product, bridged ion E. When R = Me, this rearrangement accounts for the 30% of **29** which is produced. However, when R = H ion E is symmetrical and it can only rearrange to secondary cation F. Since methyl-migrated products are not obtained from solvolysis of **21**, either rearrangement to ion E does not occur, or, if it does, the secondary ion F must react solely by deprotonation to alkene **22**.

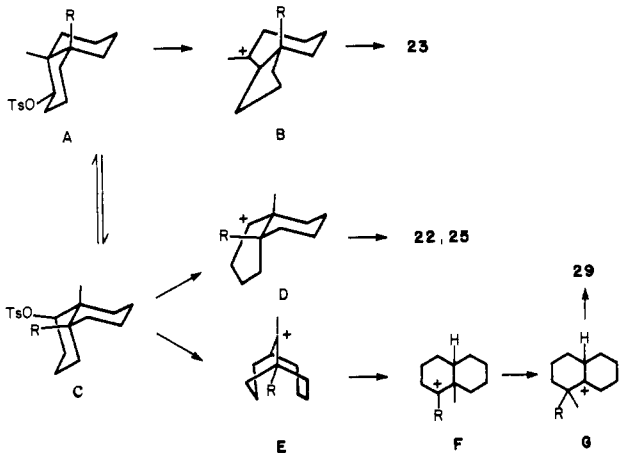
Having been thwarted in our initial attempt to prepare the pseudoguaiane skeleton by the hydronaphthalene route, we turned to the anionic pinacol rearrangement. The method was first used for the generation of the hydroazulene skeleton by Mazur and Nussim in 1961 (**30** → **31**)[23] and was subsequently employed by


30 31

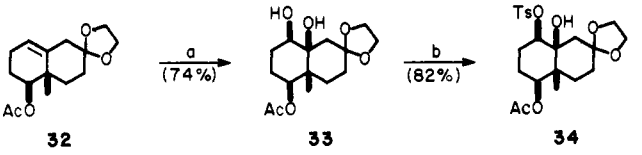
Büchi, Hofheinz, and Paukstelis in a synthesis of the guaiane sesquiterpene aromadendrene.[24] The necessary substrate for such a route to the pseudoguaianes was readily synthesized as shown in Scheme VI. The known ketal acetate **32**[25] is conveniently hydroxylated by the use of catalytic $OsO_4$ with *N*-methylmorpholine oxide as cooxidant.[26] The addition is highly stereoselective; diol **33** is the only stereoisomeric product detected in the reaction mixture. Although it was expected that addition of the bulky compound $OsO_4$ to the bottom face of the double bond would be somewhat hindered by the axial ketal oxygen, the magnitude of the stereoselectivity is surprising, since compound **32** undergoes epoxidation with *m*-chloroperoxybenzoic acid in chloroform to give a 1:1 mixture of diastereomeric epoxides.[27] Selective tosylation of diol **33** provides the crystalline tosylate **34**.

The solvolytic behavior of tosylate **34** is very interesting. If solvolysis is carried out in dry *tert*-butyl alcohol containing 2 equiv of lithium hydroxide, rearranged keto acetate **35** is obtained in 81% yield. On the other hand, if solvolysis is carried out in dry *tert*-butyl alcohol containing 2 equiv of potassium hydroxide,

Scheme V



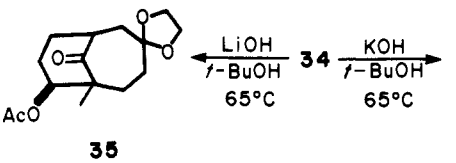

Scheme VI



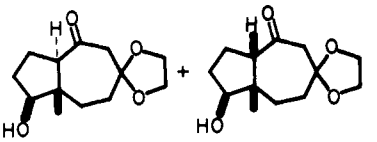

32 33 34

(a) $OsO_4$, *N*-methylmorpholine oxide, THF; (b) *p*-TsCl, pyridine, 0 °C

isomeric keto alcohols **36** and **37** are obtained in a ratio of 4:1 in 87% yield. The key to understanding these divergent results

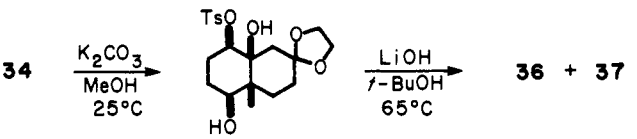



35




36 37

is the fact that the lithium hydroxide mediated rearrangement leads to a keto *acetate*, while the potassium hydroxide catalyzed reaction affords keto *alcohols*. Indeed, solvolysis of diol tosylate **38** with lithium hydroxide in *tert*-butyl alcohol gives solely **36** and **37**.



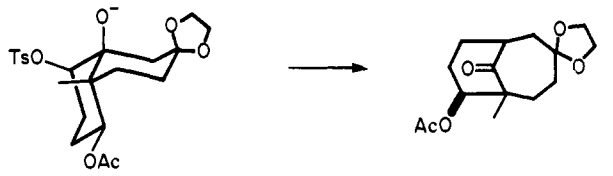

38

The results obtained from solvolysis of tosylate **34** are explicable in terms of the conformational arguments set forth in Scheme VII. We start with the assumption that productive ionization only occurs when the proximate hydroxyl is deprotonated and that ionization is accompanied by migration of the vicinal carbon–carbon bond which is anti coplanar to the tosylate. If solvolysis occurs while the acetate group is intact, we believe that it is conformation **34a** which reacts. However, if solvolysis occurs after the acetate group has been saponified, the necessary alkoxide must adopt conformation **38a** so that it can benefit from hydrogen bonding with the other hydroxyl.

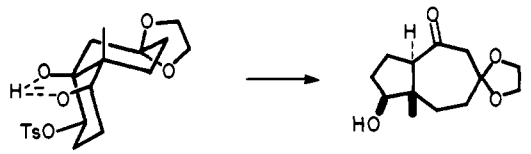
Trans-fused hydroazulenone **36** is the primary rearrangement product from **34**; isomer **37** results from base-catalyzed equilibration of **36**. In fact, the equilibrium ratio of **36**:**37** = 4:1 is close

(23) Y. Mazur and N. Nussim, *J. Am. Chem. Soc.*, **83**, 3911 (1961).
(24) G. Büchi, W. Hofheinz, and J. V. Paukstelis, *J. Am. Chem. Soc.*, **91**, 6473 (1969).
(25) C. H. Heathcock and R. Ratcliffe, *J. Am. Chem. Soc.*, **93**, 1746 (1971).
(26) V. Van Rheenen, R. C. Kelly, and D. Y. Cha, *Tetrahedron Lett.*, 1973 (1976).
(27) C. H. Heathcock and R. A. Badger, *J. Org. Chem.*, **37**, 234 (1972).

Scheme VII

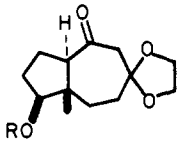


**34a** **35**



**38a** **36**

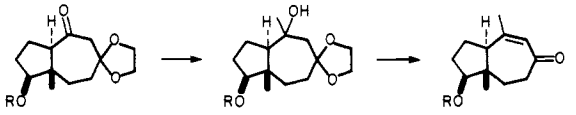
to the ratio observed in similar systems.[5a,28] On a small scale, taking care to use just 1 equiv of KOH in *tert*-butyl alcohol, we have been able to accomplish the rearrangement of **38** to **36**, without subsequent cis–trans equilibration. However, we have not been able to work out a reliable procedure for doing this on a reasonable scale. The crystalline acetate and benzoate esters of alcohol **36** (**39** and **40**, respectively) may be readily obtained,



**39**: R = $COCH_3$
**40**: R = $COC_6H_5$

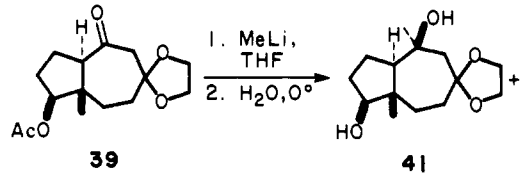
either by recrystallization or preparative HPLC of the mixture of esters. If desired, the remaining acetate of the cis diastereomer **37** may be equilibrated to obtain the original 4:1 mixture of **36** and **37**.

At this point in the synthesis, we had planned to convert the 1,3-dione monoketal into a $\beta$-methyl-$\alpha,\beta$-unsaturated ketone by methylation, followed by acid-catalyzed hydrolysis (eq 5).

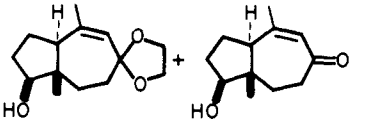


(5)

However, the realization of this seemingly trivial transformation proved to be no simple matter. Rapid addition of excess methyllithium to keto acetate **39**, followed by *nonacidic* workup, provides 80% of diol **41** and 20% of a mixture of unsaturated ketal **42** and enone **43**. If the methyllithium is added to keto acetate



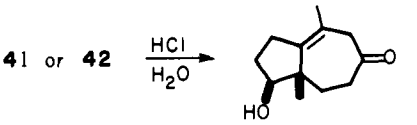
**39** **41**



**42** **43**

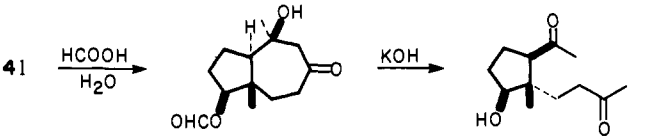
(28) J. A. Marshall and G. B. Ellison, *Synthesis*, 517 (1972).

**39** slowly (over a 15-min period), diol **41** is the minor product (25%), while **42** and **43** constitute 75% of the reaction mixture. Acidic hydrolysis of the product mixture of pure **41**, or of unsaturated ketal **42** gives completely the $\beta,\gamma$-unsaturated ketone **44**. Diol **41** can be hydrolyzed without dehydration by the use



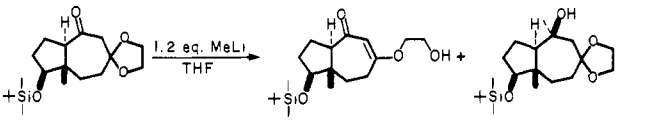
**44**

of aqueous formic acid. However, attempts to dehydrate the resulting $\beta$-hydroxy ketone **45** under a variety of acidic conditions led only to enone **44**. An attempt to bring about base-catalyzed dehydration of **45** resulted in retroaldolization to afford crystalline dione **46**.



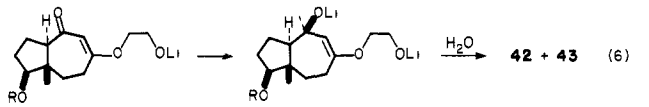
**45** **46**

The source of the unexpected products **42** and **43** in the methylation of **39** became clear when we added 1.2 equiv of methyllithium to the keto ether **47**. In this reaction, enol ether **48** and alcohol **49** are produced in a 60:40 ratio. It would seem from



**47** **48** **49**

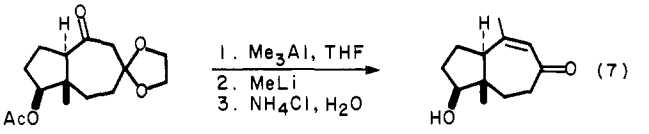
this result that base-catalyzed elimination of the $\beta$-alkoxy group competes with addition of methyllithium to the carbonyl. When excess methyllithium is used, addition to the enone occurs, and this product might lead to **42** and **43** on workup (eq 6). The effect



(6)

of addition time on the amount of **42** and **43** produced in the reaction may be due to the fact that under the slow addition conditions, the methyllithium concentration is lower, and more time is available for the alkoxides which are produced in the reactions to bring about the $\beta$-elimination reaction.

We were able to capitalize on this hypothesis as shown in eq 7. Keto acetate **39** is treated with 1 equiv of trimethylaluminum



(7)

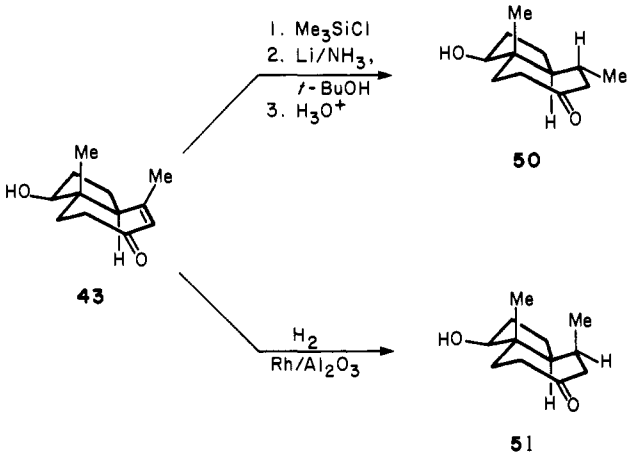
**39** **43**

in THF at 0 °C, followed by excess methyllithium. After a brief reaction period, the mixture is quenched with aqueous ammonium chloride, whereupon enone **43** is produced in about 70% yield. This is a reliable procedure, which we have carried out several times on a several gram scale.

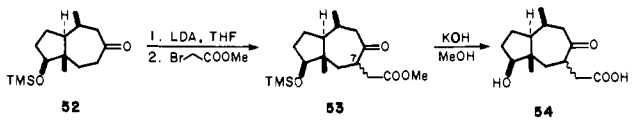
As expected, lithium/ammonia reduction of the trimethylsilyl ether of **43** gives solely the 10$\alpha$ methyl hydroazulenone **50**[10b] while catalytic hydrogenation gives the nicely crystalline 10$\beta$ diastereomer **51**.

Since hydroxy ketone **50** has been converted into (±)-helenalin by Roberts and Schlessinger,[10a] the obtention of this intermediate formally provides a third total synthesis of this helenanolide.[6c,10]

For the synthesis of (±)-confertin, the trimethylsilyl ether of hydroxy ketone **51** is alkylated with methyl bromoacetate; keto

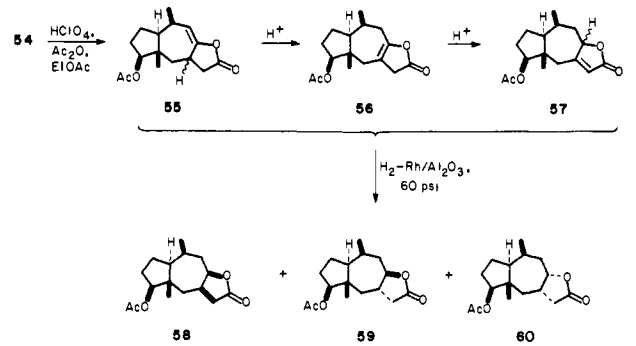



esters **53** are obtained as a 4:1 mixture of diastereomers in 75%




yield. Schlessinger and co-workers have observed similar regioselectivity in deprotonation of compounds related to **52**.[10] Treatment of this mixture of keto esters with methanolic KOH gives keto acids **54** in quantitative yield.

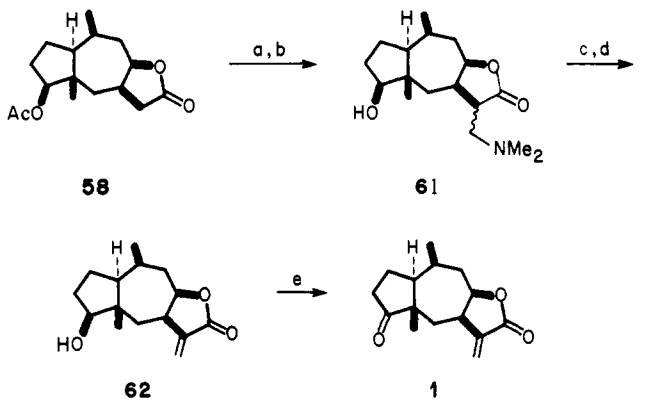
Exposure of keto acids **54** to methanesulfonic acid in acetic anhydride for 1 h at room temperature gives a diastereomeric mixture of enol lactones **55**. When more acidic conditions are employed, enol lactone **55** isomerizes to enol lactone **56** which, in turn, isomerizes to butenolide **57**. By carefully monitoring the course of this complex series of isomerizations, it is possible to maximize the yield of the desired enol lactone **56**. Catalytic hydrogenation of the mixture of isomers at this point gives the crystalline lactone **58** in 34% yield (from keto ester **53**), along with 9% of a mixture of lactones **59** and **60**.




The stereostructures of isomeric lactones **58–60** were inferred from their 250-MHz $^1$H NMR spectra. The lactone carbinol resonance in **58** occurs at essentially the same chemical shift (4.72 ppm) as seen in confertin (4.65 ppm) and shows the same splitting pattern as the analogous resonance in the natural product.[29] The $^1$H NMR spectra of isomers **59** and **60** are substantially different. In one isomer, the lactone carbinol resonance appears as a triplet with $J$ = 10 Hz at 4.16 ppm. The large coupling constant suggests that this resonance is due to a trans-fused lactone, and the isomer giving rise to it is assigned structure **59**. This product must arise from hydrogenation of either **55** or **57**. The other saturated lactone shows the lactone carbinol resonance as a complex multiplet at $\delta$ 4.96. This isomer is assumed to be the other cis-fused lactone and also must arise from hydrogenation of one of the isomers of either **55** or **57**, since Schlessinger reports the formation of only one cis-fused lactone upon hydrogenation of **56**.[10b] Catalytic hydrogenation of enol lactone **55** provides **58**, **59**, and **60** in yields of 29%, 31%, and 19%, respectively.

(29) H. Yoshioka, T. S. Mabry, and B. N. Timmerman, "Sesquiterpene Methylene Lactones", University of Tokyo Press, Tokyo, Japan, 1973.

Scheme VIII




(a) KOH, MeOH; (b) LDA, DME, $Me_2\overset{+}{N}=CH_2I^-$; (c) MeI; (d) $NaHCO_3$; (e) Jones

Lactone ester **58** was converted into (±)-confertin as shown in Scheme VIII. Saponification of **58** gives a hydroxy lactone, which is alkylated with Eschenmoser's salt[30] by the procedure of Danishefsky.[31] After quaternization and elimination of trimethylamine, followed by Jones oxidation, (±)-confertin (**1**) is obtained in 31% overall yield for the five-step sequence.

In summary, we have explored the Wagner–Meerwein rearrangement of suitable dimethyldecalyl tosylates as a method for constructing the pseudoguaiane skeleton and found it to be unsuitable for this purpose. The anionic pinacol rearrangement provides ready entry to the pseudoguaianes, and we have worked out a 16-step total synthesis of (±)-confertin which proceeds in 2.7% overall yield from the known ketal acetate **32**. Compared to the other successful syntheses of **1**,[3] our synthesis is reasonable in length, but it is not outstanding in overall yield. For example, the Schlessinger synthesis of **1**, which requires 17 steps from a material more-or-less comparable to **32**, is reported to proceed in 15% overall yield. Much of this yield superiority has to do with the conversion of ketone **52** into lactone **58** (63% in the Schlessinger synthesis, 34% in our synthesis).

## Experimental Section

Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Ether, 1,2-dimethoxyethane (DME) and tetrahydrofuran (THF) were distilled from sodium benzophenone immediately before use. All reactions were carried out under an atmosphere of dry nitrogen. Boiling points and melting points (Pyrex capillary) are uncorrected. Infrared spectra (IR) were determined on Perkin-Elmer Model 137 and 297 spectrometers, UV spectra were determined on a Cary Model 118 instrument, results are expressed as $\lambda_{max}$ in nm (log $\epsilon$). $^1$H NMR were determined on the following instruments: Varian T-60, Varian EM-390, Perkin-Elmer Hitachi R-24B or UCB 250 (a superconducting 250-MHz FT machine). Chemical shift data are reported in parts per million downfield from internal tetramethylsilane. $^1$H NMR data are tabulated as follows: chemical shift (number of protons, multiplicity, coupling constant in hertz). Mass spectral data were obtained with Atlas MS-12 and Consolidated 12-110B spectrometers and are tabulated as $m/e$ (intensity as percent of total ion current). Gas–liquid partition chromatography (GPLC) was carried out with the indicated column and temperature using a Varian 920 or 940 instrument. High-performance liquid chromatography (HPLC) was carried out on the Waters Prep LC/System 500. Elemental analyses were performed by the Microanalytical Laboratory operated by the College of Chemistry, University of California, Berkeley, CA. Unless otherwise noted solvents were dried with anhydrous magnesium sulfate prior to evaporation of the solvent at reduced pressure using a rotary evaporator.

**(6*SR*,7*SR*)-7-((*tert*-Butyldimethylsilyl)oxy)-6-methylbicyclo[4.4.0]-dec-1-en-3-one (6).** Dione **5a** was reduced by the published procedure[32]

(30) J. Schreiber, M. Haag, N. Hashimoto, and A. Eschenmoser, *Angew. Chem., Int. Ed. Engl.*, **10**, 330 (1971).

(31) (a) S. Danishefsky, T. Kitahara, R. McKee, and P. F. Schuda, *J. Am. Chem. Soc.*, **98**, 6715 (1976); (b) S. Danishefsky, P. F. Schuda, T. Kitahara, and S. J. Etheredge, *ibid.*, **99**, 6066 (1977).

(32) C. H. Heathcock, R. A. Badger, and J. W. Patterson, Jr., *J. Am. Chem. Soc.*, **89**, 4133 (1967).

to obtain the corresponding keto alcohol. To a solution of 18 g (0.1 mol) of this material in 40 mL of DMF was added 18.05 g (0.12 mol) of *tert*-butylchlorodimethylsilane and 17 g (0.25 mol) of imidazole. This solution was stirred under nitrogen for 64 h and then diluted with 200 mL of water. This mixture was extracted three times with ether, and the combined ether extracts were washed with 10% HCl (three times), sodium bicarbonate, and brine. Evaporation of the solvent left 29.0 g (98%) of a clear red oil. The analytical sample (mp 65–66 °C) was obtained by chromatography of the crude oil on silica gel and recrystallization of the resulting solid from aqueous ethanol: IR (film) 3000, 2900, 1675, 1625, 1460 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.07 (6 H, s), 0.90 (9 H, s), 1.19 (3 H, s), 3.42 (1 H, m), 5.78 (1 H, s). Anal. Calcd for $C_{17}H_{30}O_2Si$: C, 69.33; H, 10.27. Found: C, 69.08; H, 10.19.

**(1*RS*,6*SR*,7*SR*)-7-((*tert*-Butyldimethylsilyl)oxy)-1,6-dimethylbicyclo[4.4.0]decan-3-one (7).** To a slurry of cuprous iodide (27.24 g, 0.143 mol) in ether at 0 °C was added 124 mL of a methyllithium solution (2.3 M in ether, 0.29 mol). This solution was stirred for 15 min, and then 26 g (0.095 mol) of enone **6** in ether was added over a period of 10 min. This mixture was stirred for another hour at room temperature and then poured into aqueous ammonia/ammonium chloride. The ether layer was separated and washed with water and brine. Evaporation of the solvent left 26 g of a dark orange oil. Analysis of this material by GLPC showed that it was a 60:40 mixture of ketone **7** and the 1,2-addition product. The 1,2-addition product, which is quite unstable, has the following $^1H$ NMR spectrum: ($CDCl_3$) $\delta$ 1.05 (3 H, s), 1.28 (3 H, s), 5.35 (1 H, s). Ketone **7** was purified by forming its bisulfite addition product with aqueous sodium bisulfite and then triturating this mixture with hexane to remove impurities. The bisulfite adduct was decomposed in aqueous sodium hydroxide, and the recovered ketone was extracted into ether: IR (film) 3000, 1725, 1470, 1260, 1085; $^1H$ NMR ($CDCl_3$) $\delta$ 0.05 (6 H, s), 0.87 (12 H, s), 0.93 (3 H, s), 4.08 (1 H, m). Anal. Calcd for $C_{18}H_{34}O_2Si$: C, 69.62; H, 11.04. Found: C, 69.81; H, 10.78.

**(1*SR*,6*RS*,7*RS*)-4-Benzylidine-7-((*tert*-butyldimethylsilyl)oxy)-1,6-dimethylbicyclo[4.4.0]decan-3-one (8).** A solution of the foregoing crude reaction mixture (containing 2 g, 3.96 mmol of **7**) in 6 mL of ethanol and 0.4 mL of water was treated with 1.5 mL of 15% sodium hydroxide and 0.45 mL (4.44 mmol) of benzaldehyde. The reaction was allowed to stand for 16 h at room temperature and 24 h in the refrigerator. After this time, the semisolid reaction mixture was filtered and washed with 70% ethanol. The yield was 1.2 g (78%) of light yellow crystals, mp 117–119 °C. The analytical sample, mp 119–120 °C, was obtained by two recrystallizations from aqueous ethanol: IR ($CDCl_3$) 2990, 1680, 1600, 1440, 836, 795 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ −0.43 (3 H, s), −0.07 (3 H, s), 0.67 (9 H, s), 1.07 (3 H, s), 1.10 (3 H, s), 2.10 (1 H, dd, A portion of AB, $J$ = 18 Hz), 2.47 (1 H, dd, A portion of ABX, $J_{AB}$ = 17, $J_{AX}$ = 3 Hz), 2.97 (1 H, dd, B portion of AB, $J$ = 18 Hz), 3.37 (1 H, dd, B portion of ABX, $J_{AB}$ = 17, $J_{BX}$ = 1.5), 3.82 (1 H, m), 7.43 (5 H, m), 7.59 (1 H, dd, X portion of ABX, $J_{AX}$ = 3, $J_{BX}$ = 1.5 Hz). Anal. Calcd for $C_{25}H_{38}O_2Si$: C, 75.32; H, 9.61. Found: C, 75.26; H, 9.54.

**(1*SR*,3*RS*,6*RS*,7*RS*)-3-Acetoxy-4-benzylidine-7-((*tert*-butyldimethylsilyl)oxy)-1,6-dimethylbicyclo[4.4.0]decan-4-one (9).** To a solution of 12.5 g of **8** (31.35 mmol) in 200 mL of THF and 34 mL of methanol was added 0.51 g (13.41 mmol) of sodium borohydride. The reactants were stirred together for 165 min and then poured into ice water. This mixture was extracted three times with ether, and the combined ether extracts were washed with brine and dried over magnesium sulfate. Evaporation of the solvents left 14 g of a thick orange oil. This oil was dissolved, with heating, in 80 mL of acetic anhydride and 5 mL of pyridine. The solution was then stirred for 24 h at room temperature and poured into cold sodium bicarbonate. This mixture was extracted with ether–hexane, and then the organic extracts were washed with brine and dried. Evaporation of the solvents left 15.1 g (100%) of a thick orange oil that was nearly homogeneous by TLC. The analytical sample, mp 92–94 °C, was obtained by crystallization from aqueous ethanol: IR ($CDCl_3$) 2950, 2930, 2880, 2860, 1740, 1250 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ −0.47 (3 H, s), −0.12 (3 H, s), 0.58 (9 H, s), 0.82 (3 H, s), 1.10 (3 H, s), 3.68 (1 H, m), 5.65 (1 H, m), 6.50 (1 H, br s), 7.22 (5 H, s). Anal. Calcd for $C_{27}H_{42}O_3Si$: C, 73.26; H, 9.56. Found: C, 72.96; H, 9.38.

**(1*SR*,3*RS*,6*RS*,7*RS*)-3-Acetoxy-7-((*tert*-butyldimethylsilyl)oxy)-1,6-dimethylbicyclo[4.4.0]decan-4-one (10) and Its $C_3$ epimer.** Ozone was passed through a −70 °C solution of **9** (13.3 g, 30 mmol) in ethyl acetate/methanol/hexane (3:6:1) until the solution turned blue (3 h). The excess ozone was purged with nitrogen at 0 °C. The solution was then cooled to −70 °C, and 8.9 mL of dimethyl sulfide was added. This mixture was allowed to stir for 2 days at room temperature, and the solvents were then evaporated. The residual oil was taken up in hexane/ether and washed with HCl, sodium bicarbonate, water, and brine. Evaporation of the solvents left 14.6 g (100%) of the crude ketone. Recrystallization from aqueous ethanol yielded 8.63 g (78%) of material, mp 76–85 °C. The $^1H$ NMR spectrum of this material indicated it to be a 3:1 mixture of **10** and its $C_3$ epimer: IR (film) 3000, 1750, 1730, 1470 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.03 (6 H, s), 0.11 (6 H, s, silyl methyls of minor isomer), 0.90 (12 H, s), 1.22 (3 H, s, angular methyl of minor isomer), 1.27 (3 H, s, angular methyl of **10**), 2.15 (3 H, s), 3.45 (1 H, m), 5.42 (1 H, dd with $J$ = 13 and 7 Hz). Anal. Calcd for $C_{20}H_{36}O_4Si$: C, 65.17; H, 9.84. Found: C, 64.88; H, 9.66.

**(1*SR*,6*RS*,7*RS*)-7-((*tert*-Butyldimethylsilyl)oxy)-1,6-dimethylbicyclo[4.4.0]decan-4-one (11).** To a solution of lithium (0.38 g, 5.43 mmol) in 100 mL of ammonia (distilled from sodium) was added 2.0 g of **10** (5.43 mmol) in 30 mL of ether. The reaction was allowed to stir for 75 min and was then quenched by slow addition of solid ammonium chloride (5.81 g, 108.6 mmol). This mixture was stirred for 30 min, and the ammonia was then evaporated. More ether and hexane were added to the mixture, which was then washed with water and brine. Evaporation of the solvents left 1.76 g (100%) of a yellow oil. The analytical sample was obtained by GLPC on 5% Carbowax at 200 °C: IR (film) 3000, 1720, 1460, 1260 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.00 (3 H, s), 0.03 (3 H, s), 0.90 (12 H, s), 1.15 (3 H, s), 3.52 (1 H, s). Anal. Calcd for $C_{18}H_{34}O_2Si$: C, 69.62; H, 11.04. Found: C, 69.39; H, 10.86.

**(1*SR*,6*RS*,7*RS*)-1,6-Dimethyl-7-hydroxybicyclo[4.4.0]decan-4-one (12).** A solution of 0.5 g of **11** (1.61 mmol) in 15 mL of THF and 5 mL of 45% HF was made up in a plastic test tube and capped. After 48 h the reaction was neutralized with sodium hydroxide and diluted with ether. The ether layer was separated and washed with water and brine. Evaporation of the solvents left 0.36 g (100%) of a light colored oil. The GLPC showed that the material was 97% pure **12**. This oil was used in subsequent reactions without further purification: IR (film) 3500, 2990, 1715, 1450 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.95 (3 H, s), 1.17 (3 H, s), 3.53 (1 H, m).

**(1*SR*,6*RS*,7*RS*)-7-(Tosyloxy)-1,6-dimethylbicyclo[4.4.0]decan-4-one (13).** To a solution of 3.0 g of **12** (15.3 mmol) in 75 mL of pyridine at 0 °C was added 5.83 g (30.6 mmol) of *p*-toluenesulfonyl chloride. The reaction was allowed to proceed for 5 days at 0 °C. At the end of this time the solution was poured into ice water and stirred for 1 h. The crystalline product was filtered, washed with water, and dried. The yield was 3.0 g (56%) of light tan powder, mp 106–112 °C. The analytical sample, mp 131–132 °C, was obtained by recrystallization from ether–hexane: IR ($CDCl_3$) 3080, 1720, 1600, 1225 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.89 (3 H, s), 1.13 (3 H, s), 2.45 (3 H, s), 4.57 (1 H, m), 7.39 (2 H, A portion of $A_2B_2$, $J_{AB}$ = 8), 7.88 (B portion of $A_2B_2$, $J_{AB}$ = 8). Anal. Calcd for $C_{19}H_{26}O_4S$: C, 65.11; H, 7.48; S, 9.15. Found: C, 64.93; H, 7.41; S, 8.98.

**a. Solvolysis of Keto Tosylate 13. In Methanol.** A solution of 0.2 g of **13** (0.57 mmol) in 11.4 mL of absolute methanol was heated to 60 °C under nitrogen for 2 h. After this time the solution was evaporated and the residual oil was taken up in ether. The ether solution was washed with sodium hydroxide, water, and brine. Evaporation of the solvent left 0.11 g of a clear oil. Analysis by GLPC (5% Carbowax, 190 °C) showed that material was mainly ether **14** (78%), along with 7.4% of enone **15** and 10% of cyclopropyl ketone **16**. An analytical sample of **16** was obtained by preparative GLPC: IR ($CDCl_3$) 2970, 1710, 1440, 1110 $cm^{-1}$; $^H$ NMR ($CDCl_3$) $\delta$ 0.92 (3 H, s), 1.16 (3 H, s), 2.17 (1 H, d, $J$ = 14.1 Hz), 2.28 (1 H, d, $J$ = 14.1 Hz), 2.51 (1 H, dd, $J$ = 14.2, 4.0 Hz), 2.61 (dd, $J$ = 14.2, 2.0 Hz), 2.96 (1 H, dd, $J$ = 11.0, 4.1 Hz), 3.31 (3 H, s). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.51; H, 10.54.

Compounds **15** and **16** were identified by GLPC comparison with authentic samples (vide infra).

**b. In Buffered Acetic Acid.** A solution of 0.2 g of **13** (0.57 mmol) and 0.11 g of potassium acetate (1.14 mmol) in 28 mL of acetic acid was held at 100 °C for 24 h. The solution was then diluted with ether and washed with water and sodium bicarbonate. Evaporation of the solvents left 0.1 g (98%) of a clear oil, shown by GLPC analysis to be 72% **15** and 28% **16**. A sample of enone **15** was obtained by preparative GLPC: IR (film) 3000, 1725, 1450 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 0.98 (3 H, s), 1.08 (3 H, s), 5.41 (1 H, A portion of $ABX_2$, $J_{AB}$ = 10, $J_{AX}$ = 1.5 Hz), 5.62 (1 H, B portion of $ABX_2$, $J_{AB}$ = 10, $J_{BX}$ = 3.0 Hz).

Wolff–Kishner reduction[22] of the mixture of **15** and **16** provides a mixture of an alkene and a saturated hydrocarbon. The alkene was identified by GLPC retention time and $^1H$ NMR spectrum as **25** (vide infra).

**1,6-Dimethyltricyclo[4.4.0.0$^{2,10}$]decan-3-one (16).** A solution of tosylate **13** (0.2 g, 0.57 mmol) and potassium *tert*-butoxide (0.064 g, 0.57 mmol) in 2 mL of *tert*-butyl alcohol was refluxed under nitrogen for 2 h. The reaction mixture was then poured into ice water and extracted with ether. The ether extract was washed with water and dried over magnesium sulfate. Evaporation of the solvents left 0.1 g (98%) of a

(33) C. H. Heathcock, J. E. Ellis, J. E. McMurry, and A. Coppolino, *Tetrahedron Lett.*, 4495 (1971).

clear oil. Analysis by GLPC showed that the oil was 93% **16** and 7% **15**. An analytical sample of **16** was obtained by preparative GLPC (5% Carbowax, 200 °C): IR (film) 2990, 1690, 1470, 1450 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.10 (3 H, s), 1.17 (3 H, s). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.80; H, 10.08.

Control experiments showed that, when pure **16** is injected into a gas chromatograph in which the inlet port is heated to 250 °C, about 5% conversion to alkene **15** occurs.

**1,6-Dimethyltricyclo[4.4.0.0$^{2,10}$]decane.** To a solution of ketone **16** (0.6 g, 3.37 mmol) in 20 mL of diethylene glycol was added 4.7 mL of 85% hydrazine hydrate. This solution was held at 120 °C under nitrogen for 3 h and then allowed to cool down. After the solution had cooled to 80 °C, 2.53 g of potassium hydroxide was added, and the solution was then heated from 102 to 210 °C over a period of 90 min while water was removed by distillation. The distillation head was then replaced with a reflux condenser, and the solution was refluxed for 3 h at 220 °C. After being cooled, the reaction mixture was recombined with the water distillate, and this solution was diluted with water and extracted with ether/hexane. The organic extracts were washed with water, dilute acid, and brine. Evaporation of the solvents left 0.53 g (95%) of a colorless oil. The analytical sample was obtained by GLPC (5% Carbowax, 150 °C): IR (film) 2990, 1470 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.57 (2 H, m), 0.93 (3 H, s), 1.01 (3 H, s); $^{13}C$ NMR ($CDCl_3$), 16.0, 16.8 (two carbons), 19.6 (two carbons), 21.0 (two carbons), 24.6, 28.5, 29.3, 34.4 (two carbons) ppm. Anal. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.85; H, 12.09.

**Diethyl [(1*RS*,6*RS*)-1,6-Dimethylbicyclo[4.4.0]dec-2-en-3-yl] Phosphate (24).** To a slurry of cuprous iodide (8.7 g, 45.7 mmol) in 100 mL of ether at 0 °C was added methyllithium (51 mL of a 1.79 M solution in ether, 91.5 mmol). After the solution was stirred for 15 min, 5 g of 6-methylbicyclo[4.4.0]dec-1-en-3-one (**5b**) was added to it. The mixture was stirred for another hour at 0 °C, and 8.8 mL (61 mmol) of chloro diethyl phosphate was added along with 10 mL of HMPT. The mixture was stirred for 3 h and then poured into aqueous ammonium chloride/ammonia. The ether layer was separated, and the aqueous phase extracted twice more with ether. The combined ether extracts were washed with water and brine. Evaporation of the solvent left 8.14 g (84%) of a clear oil. The analytical sample was obtained by GLPC (5% Carbowax, 200 °C). IR (film) 2900, 1680, 1460, 1440, 1275 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.90 (6 H, s), 1.33 (6 H, t), 4.22 (4 H, quintuplet), 5.17 (1 H, m). Anal. Calcd for $C_{16}H_{29}O_4P$: C, 60.74; H, 9.24; P, 9.79. Found: C, 60.86; H, 8.99; P, 9.71.

**(1*RS*,6*RS*)-1,6-Dimethylbicyclo[4.4.0]dec-2-ene (25).** Approximately 1 L of ethylamine was distilled from sodium into a dry flask containing 9.37 g (1.35 mol) of lithium. The flask was equipped with a dry ice cold finger and a dropping funnel containing THF (100 mL), *tert*-butyl alcohol (76 mL, 0.81 mol), and enol phosphate **24** (85 g, 0.27 mol). The substrate solution was added to the lithium over a period of 90 min, and then the mixture was stirred for an additional 20 min. The reaction was quenched by the slow addition of water. The aqueous mixture was partially neutralized with sulfuric acid in order to dissolve the lithium hydroxide. This mixture was then extracted with ether, and the ether phase was separated, dried, and evaporated. The crude yield was 57.5 g. This material was distilled (45 °C, 1 torr) to give 36 g (82%) of **25**, contaminated with a small amount of the fully saturated decalin. The analytical sample was obtained by GLPC (5% Carbowax, 130 °C): IR (film) 2900, 1650, 1460, 1440 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.88 (6 H, s), 5.23 (1 H, dt, A portion of $ABX_2$, $J_{AB}$ = 10, $J_{AX}$ = 1.5 Hz), 5.52 (1 H, dt, B portion of $ABX_2$, $J_{AB}$ = 10, $J_{BX}$ = 3.0 Hz). Anal. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.58; H, 12.13.

**(1*RS*,2*SR*,3*RS*,6*RS*)-1,6-Dimethylbicyclo[4.4.0]dec-2-ene Oxide (26).** To an ice cold solution of 5.0 g (30.5 mmol) of alkene **25** in 50 mL of chloroform was added 7.74 g (38.1 mmol) of *m*-chloroperoxybenzoic acid dissolved in 200 mL of chloroform. After the mixture was stirred overnight, 100 mL of 20% sodium sulfite was added to the reaction mixture, which was stirred for another 3 h. The two layers were separated, and the chloroform layer was washed with sodium hydroxide, dried, and evaporated. The yield was 5.2 g (95%) of a 3:1 mixture of diastereomeric epoxides, with **26** predominating. An analytical sample was obtained by preparative GLPC (5% Carbowax, 150 °C): IR (film) 2900, 1460, 1440 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) epoxide **26** $\delta$ 0.88 (3 H, s), 0.98 (3 H, s), 2.70 (1 H, d, $J$ = 4 Hz), 3.17 (1 H, m), minor isomer $\delta$ 0.78 (3 H, s), 1.03 (3 H, s), 2.58 (1 H, d, $J$ = 4 Hz), 3.17 (1 H, m). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.01; H, 11.12.

**(1*RS*,2*RS*,6*RS*)-1,6-Dimethylbicyclo[4.4.0]decan-2-ol (27).** a. A solution of 5.0 g of ketone **7** (16.1 mmol) and 18.2 mL of 85% hydrazine hydrate in 80 mL of diethylene glycol was heated under nitrogen for 2.5 h at 120 °C. The mixture was cooled slightly, and 9.89 g of potassium hydroxide was added. The temperature was raised to 210 °C over a period of 50 min while water was removed by distillation. The distillation head was replaced with a condenser, and the mixture was refluxed at 220 °C for 2.5 h. The reaction mixture was cooled and poured into water along with the distillate collected earlier. This mixture was extracted with ether and the ether layer washed with acid, water, and brine. Evaporation of the solvents left 4.46 g of an oil which consisted of a 50:50 mixture of **27** and its silyl ether. This oil was dissolved in a mixture of 30 mL of THF and 10 mL of 48% HF. After being stirred for 20 h, this solution was neutralized with sodium hydroxide and extracted with ether. Evaporation of the ether left 2.66 g (100%) of a clear oil which was shown to be pure **27** by GLPC analysis: IR (film) 3450, 2950, 1440 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.83 (3 H, s), 4.02 (1 H, m). Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.25; H, 11.99.

b. To an ice cold solution of epoxide **26** (5 g, 28 mmol) in 50 mL of ether was added 0.53 g (13.9 mmol) of lithium aluminum hydride. The reaction was stirred overnight at room temperature and then quenched with ethyl acetate. The reaction was worked up by adding 0.53 mL of water, 0.53 mL of 15% sodium hydroxide, and then another 1.6 mL of water. After stirring for 10 min, the mixture was filtered. The ether layer was separated and washed with brine. Evaporation of the solvent left 4.9 g (98%) of alcohol **27**, identical with the product prepared by the method in part A.

**(1*RS*,2*RS*,6*RS*)-1,6-Dimethylbicyclo[4.4.0]decan-2-yl *p*-Toluenesulfonate (28).** To a solution of alcohol **27** (5.56 g, 30.55 mmol) in 100 mL of pyridine was added 11.65 g (61.10 mmol) of *p*-toluenesulfonyl chloride. The solution was stirred for 40 h at room temperature and then poured into rapidly stirring ice water. After 4 h the water was extracted with ether. The ether extract was washed with 5% HCl and saturated sodium bicarbonate. Evaporation of the solvent left 10.13 g of a crude solid. Recrystallization from hexane gave 7.5 g (74%) of tosylate **28**: mp 64–66 °C; IR ($CDCl_3$) 2980, 1600, 1430 $cm^{-1}$ $^1H$ NMR ($CDCl_3$) $\delta$ 0.88 (3 H, s), 0.95 (3 H, s), 2.47 (3 H, s), 5.10 (1 H, m), 7.35 (2 H, A portion of $A_2B_2$, $J$ = 8 Hz), 7.83 (2 H, B portion of $A_2B_2$, $J$ = 8 Hz). Elemental analysis was not obtained due to rapid decomposition.

Drying of tosylate **28** over sulfuric acid in a vacuum desiccator resulted in the decomposition of the compound into a clear hexane soluble oil and a red tar. This compound also decomposed while sealed in glass vials. The clear oil was identified as alkene **29** by comparison of its $^1H$ NMR spectrum with that of authentic material (vide infra). Acetolysis of tosylate **28**[22] gave 90% yield of an oily hydrocarbon, shown by GLPC to be a 75:25 mixture of alkenes **25** and **29**.

**2,2-Dimethylbicyclo[4.4.0]dec-6(1)-ene (29).** To a solution of 0.54 g (3.27 mmol) of (1*SR*,6*SR*)-1-methylbicyclo[4.4.0]decan-2-one in 10 mL of ether was added 2.1 mL of a 1.86 M (3.9 mmol) solution of methyllithium in ether. The solution was stirred for 30 min and then poured into brine and the mixture extracted with ether. The ether extract was dried over magnesium sulfate and evaporated, yielding 0.53 g of a clear oil: IR (film) 3460, 2925, 2860, 1430, 1420 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.93 (3 H, s), 1.13 (3 H, s).

A solution of 0.53 g of this material in 10 mL of hexane was stirred in contact with 60% aqueous sulfuric acid for 1 day. The two-phase mixture was diluted with water and the hexane layer separated. The organic phase was washed with sodium bicarbonate, dried, and evaporated to give 0.5 g of a clear oil. The analytical sample was obtained by GLPC (5% Carbowax, 130 °C): IR (film) 2920, 2850, 1440; $^1H$ NMR ($CDCl_3$) $\delta$ 0.93 (6 H, s). There were no other significant peaks in the $^1H$ NMR spectrum. This compound was by $^1H$ NMR and GLPC analysis identical with the material produced by the decomposition of tosylate **28** (vide supra). Anal. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.56; H, 12.23.

**(1*SR*,2*RS*,5*SR*,6*RS*)-5-Acetoxy-9,9-(ethylenedioxy)-6-methylbicyclo[4.4.0]decane-1,2-diol (33).** To a solution of osmium tetroxide (0.5 g, 1.97 mmol) in THF (20 mL), *tert*-butyl alcohol (70 mL), and water (8 mL) was added *N*-methylmorpholine *N*-oxide (3.2 g, 20.7 mmol) and ketal acetate **32**[25] (5 g, 18.8 mmol). This solution was stirred for 48 h at room temperature and then quenched with aqueous sodium bisulfite (7 g in 100 mL). After being stirred for 1 h, the mixture was added to a slurry of 80 g of Florisil in 400 mL of water and stirred for an additional 10 min. The mixture was filtered and the Florisil washed several times with ether. The filtrate was diluted with additional water, the layers were separated, and aqueous phase was extracted three times with ether. The combined organic layers were washed with water and brine, then dried over $MgSO_4$, and evaporated to give 4.2 g (74%) of crystalline diol **33**. Recrystallization from ether afforded pure **33**: mp 152–154 °C; IR ($CDCl_3$) 3450, 2940, 1730, 1440, 1355, 1225 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.20 (3 H, s), 2.10 (3 H, s), 3.47 (2 H, s), 3.57 (1 H, br m), 4.00 (4 H, s), 5.00 (1 H, br m). Anal. Calcd for $C_{15}H_{20}O_6$: C, 59.99; H, 8.05. Found: C, 60.02; H, 8.06.

**(1*SR*,2*RS*,5*SR*,6*RS*)-5-Acetoxy-9,9-(ethylenedioxy)-6-methyl-2-((*p*-toluenesulfonyl)oxy)bicyclo[4.4.0]decan-1-ol (34).** The diol **33** (50 g, 0.17 mol) was added to a solution of *p*-toluenesulfonyl chloride (50 g,

0.26 mol) in 300 mL of pyridine which had been precooled to 0 °C. The solution was kept at room temperature for 6 days and then poured into 1.2 L of ice water and the mixture extracted with chloroform (3 × 200 mL). The combined chloroform extracts were washed with water and brine and dried over magnesium sulfate. The solution was evaporated in vacuo until crystals started to form. This mixture was then diluted with 300 mL of 1:1 ether/hexane, cooled, and filtered to obtain 62 g (82%) of crystalline tosylate **34**. Recrystallization from chloroform/ether afforded the analytical sample: mp 122–122.5 °C; IR ($CHCl_3$) 3470, 3010, 1725, 1600, 1205, 790, 710 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.05 (3 H, s), 2.03 (3 H, s), 4.58 (1 H, br m), 4.90 (1 H, br m), 7.20 (2 H, A part of $A_2B_2$, $J$ = 8 Hz), 7.73 (1 H, B part of $A_2B_2$, $J$ = 8 Hz). Anal. Calcd for $C_{22}H_{30}O_8S$: C, 58.13; H, 6.65; S, 7.05. Found: C, 58.16; H, 6.68; S, 6.84.

**Solvolysis of Tosylate 34. a. With LiOH.** To a solution of tosylate **34** (0.5 g, 1.1 mmol) in 20 mL of dry *tert*-butyl alcohol was added 39.6 $\mu$L (2.2 mmol) of water and 0.92 mL of 2.4 M butyllithium solution (2.2 mmol). The solution was stirred overnight at 65 °C, cooled to 0 °C, and then added to a water/ether mixture. The aqueous layer was separated and extracted twice more with ether. The combined organic layers were washed with brine, dried over magnesium sulfate, and evaporated to give 0.25 g (81%) of keto acetate **35** as a clear orange oil. The analytical sample was obtained by preparative TLC on silica gel using ether as the eluant: IR (film) 2950, 1730, 1720, 1445, 1240 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.07 (3 H, s), 2.00 (3 H, s), 3.93 (4 H, s), 5.05 (1 H, m). Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.57; H, 7.82.

**b. With KOH.** Potassium hydroxide (5.8 g, 88 mmol) was crushed and added to hot *tert*-butyl alcohol (400 mL), and the solution was stirred until homogeneous. The solution was cooled to ~40 °C, and tosylate **34** (20 g, 44 mmol) was added all at once. The mixture was stirred for 6 h at room temperature, then poured into brine, and extracted with ether/chloroform. Evaporation of solvent gave 9.3 g (87%) of a 4:1 mixture of **36** and **37** as an orange oil: IR (film) 3400, 2940, 1690, 1265 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.75 (3 H, s), 1.87 (2 H, s), 2.48 (1 H, br s), 2.7 (2 H, s), 3.08 (1 H, t), 3.73 (1 H, t), 3.98 (4 H, s). This material was normally purified as its acetate or benzoate ester, which were prepared by the following procedures.

A solution of the crude hydroxy ketone (62 g, 0.26 mol) in 85 mL of pyridine was treated with 48 mL (0.52 mol) of acetic anhydride. After 2 days at room temperature the reaction was poured into an ether/aqueous sodium bicarbonate mixture. The ether layer was separated, washed with sodium bicarbonate, and dried over magnesium sulfate. Evaporation of the solvent left 73 g (100%) of an orange oil. Crystallization from ether yielded 50 g (68%) of acetate **39** with a melting point of 100–104 °C. The analytical sample, mp 100–101.5 °C, was obtained by recrystallization from chloroform/ether: IR ($CDCl_3$) 2940, 1730, 1690, 1430, 1240 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.83 (3 H, s), 1.87 (2 H, s), 2.08 (3 H, s), 2.72 (2 H, s), 3.18 (1 H, t), 3.98 (4 H, d), 4.77 (1 H, t); $^{13}C$ NMR ($CDCl_3$) 12.3, 18.7, 20.7, 25.6, 33.2, 34.6, 44.2, 52.7, 56.1, 63.4, 64.8, 82.6, 107.5, 170.2, 207.1 ppm. Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.68; H, 7.85.

A 2.87-g sample (12.0 mmol) of the mixture of alcohols **36** and **37**, obtained from the rearrangement of **34**, was dissolved in 25 mL of methylene chloride at 0 °C. Pyridine (1.95 mL, 24 mmol) and benzoyl chloride (2.8 mL, 24 mmol) were added sequentially, and the cooling bath was removed.

After 18 h, the mixture was partitioned between water and ethyl acetate. The combined organic phase was washed with cold 1 N HCl, saturated sodium bicarbonate solution, and brine. After the mixture was dried, the solvent was evaporated to yield 5.3 g (128%) of an oil which was purified by HPLC, using 40% ether in hexane as eluant. The major product is benzoate **40** (2.37 g, 57%): mp 93.5–94.0 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 8.13–7.3 (5 H, m), 5.03 (1 H, t, $J$ = 8 Hz), 3.97 (4 H, s), 3.27 (1 H, *t*, $J$ = 8 Hz), 0.97 (3 H, s); IR (KBr) 1705, 1690 $cm^{-1}$. Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.68; H, 7.09. The minor product, mp 141–142 °C, is clearly a structural isomer and was assigned the structure **37** ($C_5$ benzoylated): $^1H$ NMR ($CDCl_3$) $\delta$ 8.0–7.1 (5 H, m), 4.8 (1 H, dd, $J$ = 8 Hz), 3.85 (4 H, s), 1.30 (1 H, s); IR ($CCl_4$) 1720 $cm^{-1}$; mass spectrum, *m/e* (relative intensity) 344 (0.79), 222 (4.06), 105 (58.04). Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.97; H, 7.09.

To a solution of either benzoate ester (100 mg) in 1 mL of $Me_2SO$ was added 78 $\mu$L of 7.5 M KOH. After 18 h the mixture was diluted with 10 mL of water and extracted with ether. The organic phase was washed several times with water and saturated sodium bicarbonate and dried and the solvent evaporated. In each case an identical 4:1 mixture of **36** and **37** was obtained.

**(1*SR*,2*RS*,5*SR*,6*RS*)-9,9-(Ethylenedioxy)-6-methyl-2-((*p*-toluenesulfonyl)oxy)bicyclo[4.4.0]decane-1,5-diol (38).** A solution of tosylate **34** (2 g, 4.4 mmol) in 40 mL of methanol was treated with 0.061 g (0.44 mmol) of potassium carbonate and stirred for 72 h at room temperature. The solution was evaporated to dryness, and the resulting crude solid was taken up in chloroform. The chloroform solution was washed with water, dried, and evaporated to give 2 g (100%) of crude diol **38**. An analytical sample, mp 109 °C dec, was obtained by recrystallization from chloroform/ether: IR (0.005 M in $CDCl_3$) 3580, 3510, 2950, 2900 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.23 (3 H, br s), 2.43 (3 H, s), 3.40 (1 H, m), 7.25 (2 H, A part of $A_2B_2$, $J$ = 8 Hz), 7.58 (2 H, B part of $A_2B_2$, $J$ = 8 Hz). Anal. Calcd for $C_{20}H_{28}SO_7$: C, 58.24; H, 6.84; S, 7.77. Found: C, 58.44; H, 6.92; S, 7.53.

Solvolysis of tosylate **38** in the presence of LiOH in dry *tert*-butyl alcohol under the identical conditions used for rearrangement of tosylate **34** to keto acetate **35** gives a mixture of keto alcohols **36** and **37** in 85% yield.

**Reaction of Keto Ketal 39 with Methyllithium. a. Fast Addition.** Methyllithium (9.64 mL of a 1.84 M solution in ether, 17.73 mmol) was added quickly (over 15 s) to a solution of compound **39** (1.0 g, 3.54 mmol) in 60 mL of THF. The solution, which became quite warm, was stirred under nitrogen for 30 min and then diluted with saturated brine. This mixture was extracted several times with ether, and the organic phase was dried and evaporated. The crude yield was 0.9 g (100%) of which 80% was the diol **41**. Other reactions in which the methyllithium was added more slowly (over 1 min) yielded a mixture of products with a ratio of ~2:2:1 of **41**, **42**, and **43**, respectively. Column chromatography of these mixtures on silica gel resulted in partial resolution of the components. The first fraction was pure unsaturated ketal **42**: IR (film) 3440, 2970, 2880, 1650, 1440 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.82 (3 H, s), 1.74 (3 H, d, $J$ = 1.5 Hz), 2.95 (1 H, br t), 3.68 (1 H, t), 3.92 (4 H, s), 5.50 (1 H, m). The second fraction contained both diol **41** and enone **43**. Pure **41**, obtained from the fast addition reactions, had the following properties: IR (film) 3440, 2970, 2880, 1070 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.92 (3 H, s), 1.20 (3 H, s), 3.67 (1 H, m), 3.93 (4 H, s). Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.69; H, 9.18.

**b. Slow Addition.** Methyllithium (150 mL of a 1.61 M solution in ether, 241 mmol) was added over a period of 30 min to solution of **39** (17 g, 60.3 mmol) in 600 mL of THF at 0 °C. The reaction was stirred for another hour and then diluted with saturated ammonium chloride solution. This mixture was extracted several times with ether, and the ether extracts were dried and evaporated to give 10.67 g of an orange oil. This oil was dissolved in 70% aqueous acetic acid containing a small amount of sodium acetate and heated on a steam bath for 30 min. This solution was cooled and added to saturated sodium bicarbonate, and the resulting mixture was extracted with ether. Drying over magnesium sulfate and evaporation yielded 5.5 g (47%) of an orange oil that was 65% **43** and 35% $\beta,\gamma$-enone **44**. Pure **43** (3.48 g (30%), mp 92–93 °C) was obtained by silica gel column chromatography and recrystallization from ether: IR (film) 3440, 2950, 2875, 1650 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.83 (3 H, s), 1.93 (3 H, d, $J$ = 1 Hz), 3.88 (1 H, t), 5.96 (1 H, m). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.00; H, 9.27.

**(1*RS*,2*SR*,7*SR*,8*SR*)-2,7-Dimethyl-2-hydroxy-8-(formyloxy)bicyclo[5.3.0]decan-4-one (45).** Keto acetate **39** (5 g) was converted to dihydroxy ketal **41** by the procedure presented above. The crude oil was taken up in 25 mL of 88% formic acid. A few drops of 10% sodium hydroxide were added to buffer the reaction. This solution was stirred overnight at room temperature and then evaporated to near dryness. The resulting oil was taken up in ether/methylene chloride and the solution washed with sodium bicarbonate, dried, and evaporated. The crude solid was recrystallized from chloroform/ether to give 2.64 g (62%) of **45**, mp 145–146.5 °C. A small amount of $\beta,\gamma$-enone **44** could be isolated from the mother liquors by chromatography on silica gel. Ketone **45** has the following properties: IR ($CDCl_3$) 3450, 2960, 1720, 1680, 1460 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.93 (3 H, s), 1.29 (3 H, s), 4.73 (1 H, m), 8.07 (1 H, s). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.70; H, 8.31.

**2-Methyl-2-(3-oxobut-1-yl)-3-(1-oxoeth-1-yl)cyclopentan-1-ol (46).** The keto formate **45**, 50 mg (0.21 mmol), was dissolved in 1 mL of methylene chloride, and 1 mL of 50% NaOH in water was added. The mixture was vigorously stirred for 2 h. After dilution with 10 mL of water, the product was isolated by extraction with methylene chloride. The organic phase was washed with bicarbonate solution and dried. Removal of the solvent left 45 mg (100%) of crystalline **46**: mp 37–39 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 3.66 (1 H, br t, $J$ = 6 Hz), 2.22 (6 H, s), 0.90 (3 H, s); IR (neat) 3450, 1701 $cm^{-1}$. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.92; H, 9.65.

**(1*RS*,7*SR*,8*SR*)-4,4-(Ethylenedioxy)-8-((*tert*-butyldimethylsilyl)oxy)-7-methylbicyclo[5.3.0]decan-2-one (47).** Hydroazulene **36** (4.26 g, 17.73 mmol), *tert*-butylchlorodimethylsilane (3.2 g, 21.28 mmol), and imidazole (2.89 g, 42.5 mmol) were dissolved in 10 mL of DMF and left to stand for 5 days. This solution was added to water, and the resulting mixture was extracted 3 times with ether. The combined ether extracts

were washed with 10% HCl and saturated sodium bicarbonate. The dried solution was evaporated to give 5.93 g of a yellow oil. Crystallization from aqueous ethanol gave 2.73 g (46%) of pure silyl ether **47**: mp 78–80 °C. IR (film) 2950, 2880, 2850, 1690, 1460, 1100 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.07 (6 H, s), 0.70 (3 H, s), 0.93 (9 H, s), 2.67 (2 H, s), 3.03 (1 H, m), 3.67 (1 H, m), 3.95 (4 H, s). Anal. Calcd for $C_{19}H_{34}O_4Si$: C, 64.36; H, 9.67. Found: C, 64.51; H, 9.46.

**Reaction of Keto Ketal 47 with Methyllithium.** Methyllithium (1.84 mL of a 1.84 M solution in ether, 3.38 mmol) was added all at once to a solution of ketone **76** (1.0 g, 2.82 mmol) in 50 mL of dry ether at −75 °C. The solution was stirred for another 10 min at −75 °C, and the cooling bath was then removed. The solution was stirred for an additional 30 min and was then poured into saturated brine and extracted twice with ether. The combined ether extracts were washed with water and brine, then dried, and evaporated to give 1.07 g (100%) of a crude solid identified as a 60:40 mixture of enol ether **48** and ketal **49**. Ketal **49** was assigned its structure on the basis of the similarity of its $^1H$ NMR spectrum to that of diol **41**; both compounds have their $C_7$ methyl resonance at $\delta$ 1.2 and a characteristic methylene peak at $\delta$ 2.10. Enol ether **48** was crystallized from ether yielding an analytically pure sample: mp 125–126 °C; IR ($CDCl_3$) 3340, 2950, 2930, 2850, 1618, 1590, 1470, 1460, 1450, 1260, 1200 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.08 (6 H, s), 0.77 (3 H, s), 0.92 (9 H, s), 3.85 (4 H, br s), 5.38 (1 H, s). Anal. Calcd for $C_{19}H_{34}O_4Si$: C, 64.36; H, 9.67. Found: C, 64.11; H, 9.44.

**(1*SR*,7*SR*,8*SR*)-2,7-Dimethyl-8-hydroxybicyclo[5.3.0]dec-2-en-4-one (43).** Keto acetate **39** (4.00 g, 14.19 mmol) was dissolved in 12 mL of dry THF, and the solution was cooled to 0 °C and treated with 7 mL of a 2 M solution of trimethylaluminum in toluene. After 10 min, 36 mL of a 1.6 M solution of methyllithium was added over a 2-h period while the temperature was maintained at 0 °C. After the addition was complete, the solution was transferred by cannula to a slush of 150 g of ice and 150 mL of saturated ammonium chloride solution. After 5 min the product was partitioned between 250 mL of 1 N HCl (0 °C) and 200 mL of ethyl acetate. The phases were separated, and the aqueous was extracted with ethyl acetate (2 × 100 mL). The combined organic phase was washed with 1 N HCl (150 mL) saturated bicarbonate (100 mL), and brine (100 mL). After the mixture was dried ($Na_2SO_4$), the solvent was evaporated at room temperature furnishing 2.08 g (75%) of a colorless oil, which is predominantly **43**. The enone is labile to isomerization to the $\beta,\gamma$ isomer **44** and so is generally used without purification. A small amount of the material was purified by column chromatography and recrystallization from ether to give a product with mp 92–93 °C and otherwise identical with that prepared as described above.

**(1*SR*,2*SR*,7*SR*,8*SR*)-2,7-Dimethyl-8-hydroxybicyclo[5.3.0]decan-4-one (51).** Enone **43** (2.07 g, 10.7 mmol) was dissolved in 500 mL of ethanol, and 1.0 g of 5% rhodium on alumina was added. The mixture was stirred under an atmosphere of hydrogen until hydrogen uptake ceased. The catalyst was removed by filtration and the solvent was evaporated to yield 2.10 g of an oil which was chromatographed on silica (100% ether). Ketone **50**, 1.74 g (83%), is obtained as a white solid: mp 72–73 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 3.65 (3 H, t, $J$ = 8 Hz), 0.97 (3 H, d, $J$ = 7 Hz), 0.73 (3 H, s); IR (neat) 3420, 1690 $cm^{-1}$. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.25; H, 10.01.

**(1*SR*,2*RS*,7*SR*,8*SR*)-2,7-Dimethyl-8-hydroxybicyclo[5.3.0]decan-4-one (50).** Enone **43** (0.43 g, 2.2 mmol) was dissolved in 10 mL of dry methylene chloride and cooled to 0 °C. Pyridine (0.75 mL, 9.3 mmol) and chlorotrimethylsilane (1.05 mL, 8.3 mmol) were added sequentially, and the mixture was stirred for 30 min at 0 °C. The mixture was diluted with 100 mL of ethyl acetate and washed with water (20 mL), cold 1 N HCl (10 mL), saturated sodium bicarbonate solution (10 mL), and brine (10 mL). After the mixture was dried ($Na_2SO_4$), the solvent was evaporated to afford 0.56 g (97%) of silylated product: $^1H$ NMR ($CDCl_3$) $\delta$ 5.85 (1 H, br s), 3.70 (1 H, t, $J$ = 8 Hz), 1.88 (3 H, d, $J$ = 1 Hz), 0.79 (3 H, s). The crude product, 0.38 g (1.42 mmol), was dissolved in 5 mL of THF and 1.4 mmol of dry *tert*-butyl alcohol was added. This solution was added, with stirring, over a 3-min period to a refluxing solution of 100 mg (14 mmol) of lithium metal in 50 mL of liquid ammonia. After addition was complete, stirring was continued for 5 min. Excess ammonium chloride was added to destroy residual lithium. The ammonia was allowed to evaporate, and the residue was partitioned between water and ethyl acetate. The organic phase was dried and evaporated to yield 0.39 g (100%) of an oil which was purified by chromatography on silica (15% ether/hexane). A white solid, 0.32 g (81%), was obtained: mp 79.5–81.0 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 3.47 (1 H, t, $J$ = 8 Hz), 0.91 (3 H, d, $J$ = 6 Hz), 0.58 (3 H, s); IR (KBr) 1685 $cm^{-1}$. Anal. Calcd for $C_{15}H_{28}O_2Si$: C, 67.11; H, 10.51. Found: C, 66.77; H, 10.55.

This material (0.32 g, 1.19 mmol) was dissolved in 5 mL of methanol, and 0.1 mL of 4 N HCl was added. After 1 h, TLC analysis (100% ether) indicated the silyl group to be completely cleaved (starting material, $R_f$ 0.88; product, $R_f$ 0.33). The methanol solution was diluted with ethyl acetate (100 mL) and washed with water (2 × 25 mL) and brine (1 × 25 mL). After drying and evaporation of the solvent, **50** was obtained in quantitative yield as an oil: $^1H$ NMR ($CDCl_3$) $\delta$ 3.47 (1 H, t, $J$ = 8 Hz), 0.86 (3 H, d, $J$ = 6 Hz), 0.53 (3 H, s); IR (neat) 3400, 1695 $cm^{-1}$; mass spectrum, $m/e$ (relative intensity) 196 (0.65), 178 (0.77), 97 (4.48); high-resolution mass spectrum, $m/e$ required for $C_{12}H_{20}O_2$ 196.1463, obsd 196.1457. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: 73.43; H, 10.35.

**(1*SR*,2*SR*,7*SR*,8*SR*)-2,7-Dimethyl-8-((trimethylsilyl)oxy)bicyclo-[5.3.0]decan-4-one (52).** Hydroxy ketone **51** (0.560 g, 2.84 mmol) was dissolved in 20 mL of methylene chloride, and 5 mL of pyridine was added, followed by 1.2 mL (9.5 mmol) of chlorotrimethylsilane. After 2 h the mixture was diluted with 50 mL of ether and washed with cold 1 N HCl (2 × 30 mL), 10% sodium bicarbonate solution (1 × 20 mL), and brine. Evaporation of solvent left 0.761 g (100%) of a solid (mp 60–61 °C). Recrystallization from petroleum ether at −60 °C furnished material of analytical purity: mp 60–61 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 3.55 (1 H, t, $J$ = 7 Hz), 0.95 (3 H, d, $J$ = 7 Hz), 0.70 (3 H, s), 0.12 (9 H, s); IR (KBr) 1680 $cm^{-1}$. Anal. Calcd for $C_{15}H_{28}O_2Si$: C, 67.11; H, 10.51. Found: C, 67.20; H, 10.14.

**Methyl [(1*SR*,2*SR*,7*SR*,8*SR*)-2,7-Dimethyl-4-oxo-8-((trimethylsilyl)oxy)bicyclo[5.3.0]dec-5-yl]acetate (53).** To a cold (−65 °C) solution of 1.39 mmol of LDA in 3 mL of 3:1 DME/hexane was added a solution of 0.339 g (1.26 mmol) of **52** in 1 mL of DME, dropwise, over a 10-min period. After 30 min, the cooling bath was removed and stirring was continued for 30 min. After the mixture was recooled to −65 °C, 0.12 mL of methyl bromoacetate (1.4 mmol) was added, the cooling bath was removed and stirring was continued for 2 h. The reaction mixture was partitioned between 1 N HCl and ethyl acetate. The aqueous phase was extracted with ethyl acetate, the combined organic phase was washed with saturated sodium bicarbonate solution and brine, and dried. Evaporation of the solvent left 430 mg of an oil. Chromatography on silica gel (25% ether/hexane) afforded **53** (0.240 g, 56%) as a mixture of $C_5$ epimers: $^1H$ NMR ($CDCl_3$) $\delta$ 3.63 (3 H, s), 1.00 (3 H, d, $J$ = 7 Hz), 0.83 and 0.70 (3 H, s, the angular methyl group in the major and minor isomers, respectively); mass spectrum, $m/e$ (relative intensity) 340 (0.78), 325 (0.43), 129 (5.86). Anal. Calcd for $C_{18}H_{32}O_4Si$: C, 63.49; H, 9.47. Found: C, 63.46; H, 9.18.

A second material was eluted from the column with 100% ether. This material showed very similar spectral properties to **53** except for the absence of a silyl group. Silylation of this byproduct afforded an additional 19% yield of **53** (total yield, 75%).

**[(1*SR*,2*SR*,7*SR*,8*SR*)-2,7-Dimethyl-8-hydroxy-4-oxobicyclo[5.3.0]-dec-5-yl]acetic acid (54).** In a preparation of keto ester **53** from 1.16 g of ketone **52** (4.33 mmol) the silyl group was completely cleaved by a prolonged workup. The crude alcohol obtained in this way (1.16 g, 100%) was dissolved in 15 mL of methanol and 1.2 mL of 7.6 M KOH solution (9.1 mmol) was added. The mixture was stirred for 3 h at room temperature. The mixture was diluted with water (50 mL), and 4 N HCl was added until the solution was pH 1. The product was extracted with ethyl acetate. The organic phase was washed with 1 N HCl which had been saturated with brine. After the mixture was dried ($Na_2SO_4$), the solvent was evaporated to yield 1.10 g (100%) of an off-white foam. Crystallization of a small amount from hot chloroform gave a microcrystalline material: mp 150–151 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 7.67 (br s, hydroxylic protons), 0.96 (3 H, d, $J$ = 7 Hz), 0.87 (3 H, s); IR (KBr) 3300, 1710, 1690 $cm^{-1}$; mass spectrum, $m/e$ (relative intensity) 254 (0.19), 236 (0.42), 124 (4.99); high resolution mass spectrum, $m/e$ required for $C_{14}H_{22}O_4$, 254.1518, found 254.1515.

**(1*SR*,2*SR*,10*SR*,11*SR*)-11-Acetoxy-2,10-dimethyl-6-oxo-5-oxatricyclo[8.3.0.0$^{4,8}$]tridec-3-ene (55).** Keto acid **54** (123 mg, 0.48 mmol) was dissolved in 1.5 mL of acetic anhydride, and 8.5 $\mu$L of methanesulfonic acid was added. After 1 h, complete conversion of the starting material ($R_f$ 0.27, 1% HOAc/ether) to a single product ($R_f$ 0.30, 50% ether/hexane) was indicated by TLC analysis. The mixture was poured into 50 mL of $NaHCO_3$ and stirred until $CO_2$ evolution ceased. The aqueous phase was extracted with chloroform (2 × 10 mL), and the organic phase was dried by filtration through $Na_2SO_4$. After evaporation of the solvents, a semisolid, 128 mg (95%) was obtained which was chromatographed on silica, eluting with 50% ether/petroleum ether. Analytically pure **55**, 84 mg (62%) was obtained (mp 112–114 °C): $^1H$ NMR ($CDCl_3$) $\delta$ 5.58 (1 H, dd, $J$ = 3 and 8 Hz), 4.65 (1 H, t, $J$ = 8 Hz), 2.03 (3 H, s), 1.08 (3 H, d, $J$ = 7 Hz), 1.00 (3 H, s); IR ($CDCl_3$) 1800, 1725 $cm^{-1}$; mass spectrum, $m/e$ (relative intensity) 278 (4). Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.95; H, 8.10.

**(1*SR*,2*SR*,4*RS*,8*RS*,10*SR*,11*SR*)-11-Acetoxy-2,10-dimethyl-6-oxo-5-oxatricyclo[8.3.0.0$^{4,8}$]tridecane (58).** Keto acid **54** (1.10 g, 4.3 mmol) was dissolved in 7.5 mL of ethyl acetate and cooled to 0 °C. Acetic anhydride (2.5 mL) was added, followed by 0.12 mL of 70% $HClO_4$. After 75 min at 0 °C the reaction mixture was diluted with 60 mL of

saturated sodium bicarbonate solution. After gas evolution ceased, the product was isolated by ethyl acetate extraction and the organic extracts were washed with sodium bicarbonate solution and brine. After the mixture was dried ($Na_2SO_4$), the solvent was evaporated to yield 1.06 g of a dark brown oil composed of several products as indicated by TLC analysis. Attempted chromatography of the mixture leads to decomposition of some or all of the products. The crude mixture was therefore used without purification or complete characterization. The presence of **55** was shown by $^1H$ NMR spectroscopy ($\delta$ 5.58, dd, $J$ = 3 and 8 Hz). The observation of a resonance at $\delta$ 5.72 (br s) suggested that the butenolide **57** was also formed in this reaction. Several absorbances are observed in the region from $\delta$ 1.0–0.8 and are not readily assigned to a particular product. A portion of the crude reaction mixture containing **56** (0.90 g) was dissolved in 50 mL of ethyl acetate, and 0.40 g of 5% rhodium on alumina was added. The mixture was shaken under 60 psi of hydrogen for 6 h. The catalyst was removed by filtration, and the solvent was evaporated. The material was chromatographed on 25 g of silica gel using 50% ether in hexane as eluant. A less polar material ($R_f$ 0.13) was eluted weighing 96 mg (9% yield). The 250-MHz $^1H$ NMR spectrum shows this product to be a 1:1 mixture of two compounds **59** and **60**: $^1H$ NMR ($CDCl_3$) $\delta$ 4.96 (1 H, m), 4.67 (1 H, t, $J$ = 8 Hz), 2.08 (3 H, s), 1.10 (3 H, d, $J$ = 7 Hz), 0.91 (3 H, s), and $\delta$ 4.15 (1 H, m), 4.56 (1 H, t, $J$ = 8 Hz), 2.08 (3 H, s), 1.00 (3 H, d, $J$ = 7 Hz), 0.95 (3 H, s); IR (neat) 1780, 1725 $cm^{-1}$.

The second material eluted ($R_f$ 0.06), **58**, was obtained as a white solid, 0.35 g (34%), mp 109.0–109.5 °C (lit.[12] 110–111 °C). The $^1H$ NMR spectrum of this compound revealed it to be closely related to confertin: $\delta$ ($CDCl_3$) 4.72 (1 H, m), 4.63 (1 H, t, $J$ = 8), 1.02 (3 H, d, $J$ = 7 Hz), 1.00 (3 H, s).

**Hydrogenation of Enol Lactone 55.** The enol lactone **55**, produced under kinetic control, 24 mg, was dissolved in 2 mL of ethyl acetate and 10 mg of 5% rhodium-on-alumina was added. The mixture was stirred under an atmosphere of hydrogen at ambient pressure and temperature for 3 h. TLC analysis (50% ether/hexane) showed the complete consumption of starting material ($R_f$ = 0.30) and the formation of two new products ($R_f$ = 0.13 and 0.06). The products were separated by chromatography on silica gel using 50% ether/hexane as eluant. The first eluted material (12 mg, 50%) was a mixture of two products as ascertained by 250 MHz $^1H$ NMR. The two products, formed in a ratio of 1.6:1, were shown by this method to be **59** and **60**, respectively. The second material eluted from the column (7 mg, 29% yield) was **58** on the basis of TLC analysis, $^1H$ NMR spectroscopy and melting point.

**(±)-Confertin (1).** Acetate **58** (0.35 g, 1.25 mmol) was dissolved in 10 mL of methanol and 0.8 mL of 7.5 M aqueous KOH was added. After 18 h at 0 °C the mixture was acidified, and stirring was continued at room temperature for 45 min. The mixture was diluted with 100 mL of ethyl acetate and washed with water, sodium bicarbonate solution, and brine. After the solution was dried ($MgSO_4$), the solvent was evaporated to yield 235 mg of the lactone alcohol (80%). Without purification, this material was dissolved in 2 mL of DME and added to a cold (−68 °C) solution of 6.3 mmol of LDA in 15 mL of 3:1 DME/pentane. After 2 h at −68 °C 1.6 g of Eschenmoser's salt[31] was added as a solid and the cooling bath was removed. After 45 min 10 mL of 4 N HCl was added. After 5 min, solid potassium carbonate was added until the solution was basic, and 20 mL of brine added. The product was isolated by extraction with chloroform (4 × 20 mL). After the organic phase was dried the solvent was evaporated and the residue taken up in 2 mL of methanol. Methyl iodide (7.5 mL) was added, and the mixture was allowed to stand for 18 h, at which time the solvents were removed in vacuo. Ethyl acetate (150 mL) was added to the resulting gum, followed by 10 mL of water and 90 mg of sodium bicarbonate. The mixture was vigorously stirred until the gum had dissolved, and the phases then were separated. An additional 50 mL of ethyl acetate was added to the aqueous phase, and stirring was continued for 5 min. The combined organic phase was dried, and the solvent was evaporated. Without purification the product was dissolved in acetone (50 mL) and titrated with Jones reagent. Excess Jones reagent was destroyed with isopropyl alcohol and the chromium salts were removed by filtration. The acetone was evaporated, and the residue was taken up in ethyl acetate and washed several times with water. After evaporation of the solvent and trituration with ether, 155 mg of a solid (mp 100–105 °C) was obtained. A portion of this material weighing 123 mg was chromatographed over 7 g of silica affording 77 mg (31%) of (±)-confertin, which was crystallized from acetone/hexane: mp 115–116 °C (lit.[9] 112–114 °C, lit.[8] 116–117 °C, lit.[10] 119–120.5 °C). The $^1H$ NMR spectrum was consistent with that reported in the literature. In addition 12 mg of normethylene confertin (5%) was also obtained: $^1H$ NMR ($CDCl_3$) 4.72 (1 H, m), 1.15 (3 H, d, $J$ = 7 Hz), 1.03 (3 H, s).

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**Registry No.** (±)-**1**, 60426-81-5; (±)-**5a** keto alcohol, 50302-16-4; (±)-**5b**, 40573-28-2; (±)-**6**, 80800-69-7; (±)-**7**, 80800-70-0; (±)-**8**, 80800-71-1; (±)-**9**, 80800-72-2; (±)-**10**, 80800-73-3; (±)-**10**, $C_3$ epimer, 80846-18-0; (±)-**11**, 80800-74-4; (±)-**12**, 80800-75-5; (±)-**13**, 80800-76-6; (±)-**14**, 80800-77-7; (±)-**15**, 80800-78-8; (±)-**16**, 80800-79-9; (±)-**17**, 80800-80-2; (±)-**18**, isomer 1, 80800-81-3; (±)-**18**, isomer 2, 80800-82-4; (±)-**19**, 80800-83-5; (±)-**24**, 80800-84-6; (±)-**25**, 80800-85-7; (±)-**26**, isomer 1, 80800-86-8; (±)-**26**, isomer 2, 80844-96-8; (±)-**27**, 80800-87-9; (±)-**28**, 80800-88-0; **29**, 80800-89-1; (±)-**32**, 73211-71-9; (±)-**33**, 80800-90-4; (±)-**34**, 80800-91-5; (±)-**35**, 80800-92-6; (±)-**36**, 80800-93-7; (±)-**37**, 80844-97-9; (±)-**38**, 80800-94-8; (±)-**39**, 80844-98-0; (±)-**40**, 80844-99-1; (±)-**41**, 80800-95-9; (±)-**42**, 80800-96-0; (±)-**43**, 80800-97-1; (±)-**43** silated, 80822-26-0; (±)-**44**, 80800-98-2; (±)-**45**, 80800-99-3; (±)-**46**, 80801-00-9; (±)-**47**, 80801-01-0; (±)-**48**, 80801-02-1; (±)-**49**, 80801-03-2; (±)-**50**, 80801-04-3; (±)-**51**, 80801-05-4; (±)-**52**, 80801-06-5; (±)-**53**, isomer 1, 80801-07-6; (±)-**53**, isomer 2, 80801-08-7; (±)-**54**, 80801-09-8; **55**, 80801-10-1; **56**, 72341-84-5; **57**, 80801-11-2; (±)-**58**, 72341-85-6; (±)-**59**, 80801-12-3; (±)-**60**, 80801-13-4; (±)-**61**, 80801-14-5; (±)-**50** TMS, 80801-15-6; (±)-1,6-dimethyltricyclo[4.4.0.$0^{2,11}$]decane, 80801-16-7; (±)-normethylene confertin, 80801-17-8; (1*SR*,6*SR*)-1-methylbicyclo[4.4.0]decan-2-one, 80845-00-7; chloro diethyl phosphate, 814-49-3; benzaldehyde, 100-52-7.