A (*Z*)-Ethylidenecyclopentane Annulation Method. Total Syntheses of (±)-Anhydrooplopanone, (±)-Oplopanone, and (±)-8-*epi*-Oplopanone

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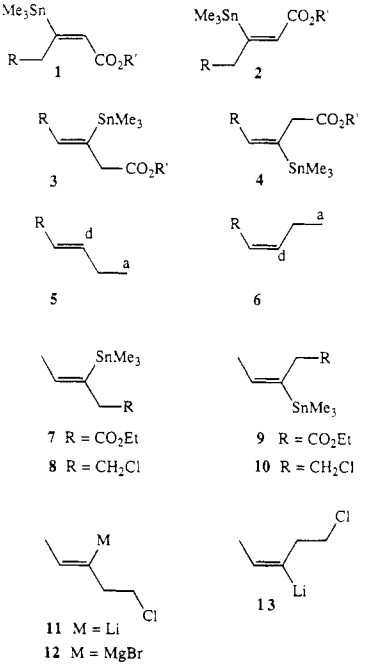
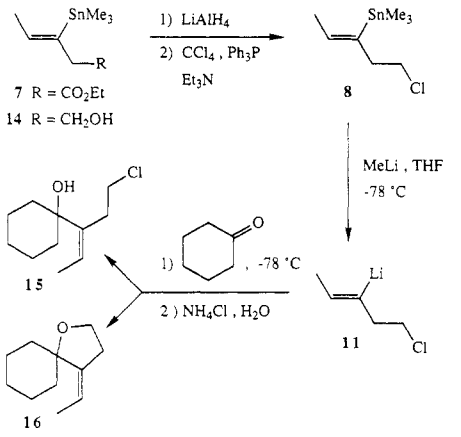
Transmetalation of (*Z*)-5-chloro-3-trimethylstannyl-2-pentene (**8**) with MeLi in tetrahydrofuran (THF) at −78 °C provides the novel bifunctional reagent (*E*)-5-chloro-3-lithio-2-pentene (**11**), which can be transformed readily into the Grignard reagent **12**. Copper(I)-catalyzed conjugate addition of **12** to cyclic α,β-unsaturated ketones (e.g., **23–29**), followed by intramolecular alkylation of the resultant chloro ketones (e.g., **30–36**), affords the corresponding (*Z*)-ethylidenecyclopentane annulation products (e.g., **37–43**). This new annulation method played a key role in total syntheses of the sesquiterpenoids (±)-anhydrooplopanone (**51**), (±)-oplopanone (**50**), and (±)-8-*epi*-oplopanone (**70**).

In the accompanying paper[1] we described the results of an investigation into the deconjugations of alkyl (*E*)- and (*Z*)-3-trimethylstannyl-2-alkenoates (**1** and **2**, respectively). Interestingly and, from a synthetic viewpoint, importantly, it was found that these conversions are stereospecific. Thus, deprotonation of substrates **1** and **2** with lithium diisopropylamide (LDA), followed by treatment of the resultant enolate anions with HOAc, provides *exclusively* the (*Z*)- and (*E*)-3-alkenoates **3** and **4**, respectively.[1] As was pointed out in the foregoing paper,[1] one of the reasons for undertaking this study concerned the possibility of using **3** and **4** as precursors of novel bifunctional reagents that would serve as synthetic equivalents to the donor–acceptor synthons[2] **5** and **6**. We report herein the results of an investigation into the transmetalations (MeLi, THF, low temperatures) of the chloro stannanes **8** and **10**, which are readily derived from the corresponding esters **7** and **9**. This study has led to the interesting discovery that, although (*Z*)-5-chloro-3-lithio-2-pentene (**13**) is too unstable

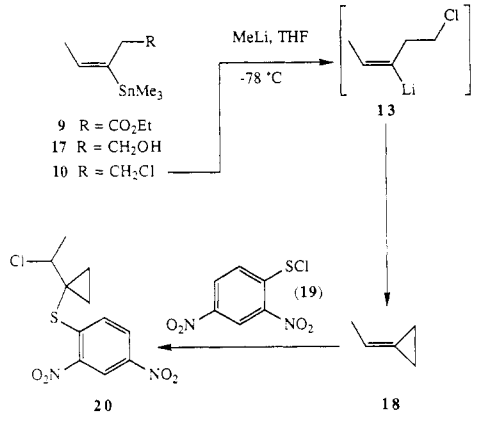


to be a useful reagent, the geometrically isomeric lithio compound **11**, along with the corresponding Grignard reagent **12**, are viable, effective bifunctional reagents. Indeed, the Grignard reagent **12** has been employed in the development of a new (*Z*)-ethylidenecyclopentane annulation method, which, in turn, has played a key role in the total synthesis of a number of oplopanane-type sesquiterpenoids. We describe below the details of this study.[3]

Scheme I



Scheme II



Results and Discussion

(a) Preparation and Transmetalation of (*Z*)- and (*E*)-5-Chloro-3-trimethylstannyl-2-pentene. Reduction of ethyl (*Z*)-3-trimethylstannyl-3-pentenoate (**7**)[1] with $LiAlH_4$, followed by reaction of the resultant alcohol **14** with CCl_4–Ph_3P–Et_3N[4,5] (Scheme I), gave the chloro

(1) Piers, E.; Gavai, A. V. *J. Org. Chem.*, preceding paper in this issue.
(2) Cf. Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.
(3) For a preliminary report, see: Piers, E.; Gavai, A. V. *Tetrahedron Lett.* **1986**, *27*, 313.
(4) Downie, I. M.; Holmes, J. B.; Lee, J. B. *Chem. Ind. (London)* **1966**, 900. Hooz, J.; Gilani, S. S. H. *Can. J. Chem.* **1968**, *46*, 86.

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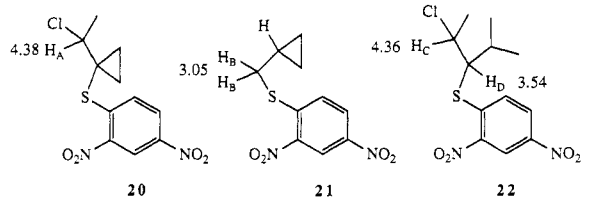
stannane **8** (78%). Treatment of **8** with MeLi in THF at −78 °C for 20 min resulted in complete disappearance of the starting material. Reaction of the resultant lithio reagent **11** with cyclohexanone (−78 °C, 45 min) afforded, after appropriate workup and flash chromatography[6] of the product mixture, the chloro alcohol **15** (31%) and the spiro ether **16** (40%). Evidently, under the reaction conditions, the lithium alkoxide corresponding to **15** underwent partial cyclization to the ether **16**. In any case, this experiment demonstrated clearly that (*E*)-5-chloro-3-lithio-2-pentene (**11**) is a viable bifunctional reagent.

Conversion of ethyl (*E*)-3-trimethylstannyl-3-pentenoate (**9**)[1] into the chloro stannane **10**, via the alcohol **17** (Scheme II), was carried out as described previously (cf. **7** → **8**, Scheme I). Transmetalation (MeLi, THF, −78 °C, 20 min) of **10** occurred smoothly, as indicated by complete consumption of the starting material. However, treatment of the reaction mixture with cyclohexanone, followed by appropriate workup, failed to produce even traces of the expected carbonyl addition product (geometric isomer of **15**) or the corresponding spiro ether (isomer of **16**). Attempts to trap the putative lithio species **13** with benzaldehyde also failed to produce any product.

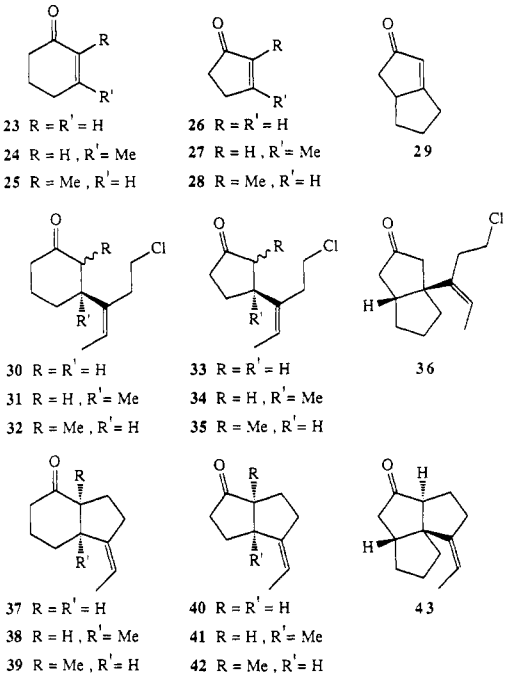
Clearly, it is reasonable to suppose that if **13** had been present in the reaction mixtures, it would have readily added to the carbonyl functions of simple substrates such as cyclohexanone and benzaldehyde. Therefore, the failure to obtain addition products indicated that **13** is very unstable, even at low temperatures (−78 °C). With respect to the fate of **13**, it seemed plausible to propose that this species self-destructs to give lithium chloride and ethylidenecyclopropane (**18**). In order to test this postulate, the reaction mixture derived from transmetalation (MeLi, THF, −78 °C) of the chloro stannane **10** was treated with a solution of 2,4-dinitrobenzenesulfenyl chloride (**19**)[7] (Scheme II), and the resultant solution was warmed slowly to room temperature. Appropriate workup, followed by recrystallization of the crude product, afforded the chloro sulfide **20** (54%). This substance, which is obviously formed from addition of the sulfenyl chloride **19** to ethylidenecyclopropane (**18**), exhibited spectral data in full accord with the assigned structure. In particular, the regiochemistry of the addition was established by the ^{1}H NMR spectrum of the product **20**, in which the proton H_A appears as a quartet (J = 7 Hz) at δ 4.38. On the basis of previously published data, it is clear from the chemical shift of this resonance that H_A is geminal to the chlorine atom and not to the 2,4-dinitrophenylthio moiety. For example, in the ^{1}H NMR spectra of compounds **21**[8] and **22** (erythro isomer),[9] the resonances due to H_B, H_C, and H_D appear at δ 3.05, 4.36, and 3.54, respectively.



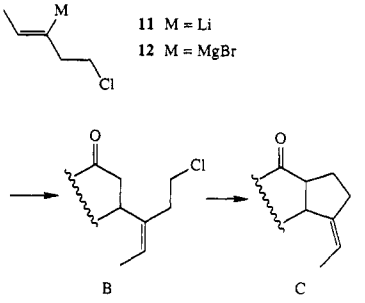
20 **21** **22**

The experiments outlined above demonstrated that (*E*)-5-chloro-3-lithio-2-pentene (**11**) is sufficiently stable at low temperatures (−78 °C) to serve as a viable bifunctional reagent. In contrast, the corresponding *Z* isomer **13** is notably less stable and, even at −78 °C, is rapidly transformed into ethylidenecyclopropane (**18**). The reason(s) underlying the difference in stability of **11** and **13** is (are) not clear. Perhaps the buttressing steric interaction between the cis Me and CH_2CH_2Cl groups in **13** is (partly) responsible for the fact that the conversion of **13** into ethylidenecyclopropane (**18**) is energetically more favorable than a similar transformation involving the lithio reagent **11**. In any case, the fact the **13** is not a viable reagent was, from a synthetic viewpoint, somewhat disappointing.

Chart I



(b) Copper(I)-Catalyzed Conjugate Addition of the Grignard Reagent 12 to Cyclic Enones. (*Z*)-Ethylidenecyclopentane Annulations. At the outset of this work, we had envisaged, inter alia, the utilization of (*E*)-5-chloro-3-lithio-2-pentene (**11**) in developing a new,

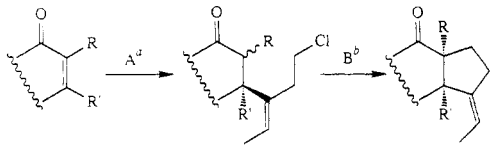


synthetically useful five-membered ring annulation method. Specifically, conjugate addition of a suitable reagent derived from **11** to cyclic α,β-unsaturated ketones (general structure A), followed by intramolecular alkylation of the resultant chloro ketones B, would, in theory, provide the (*Z*)-ethylidenecyclopentane annulation products C.

After preliminary investigations involving the use of various cuprate reagents derived from **11**, it was found that the desired conjugate addition reactions (A → B) could be accomplished conveniently by use of the Grignard reagent **12**, which is readily formed by addition of 1 equiv of $MgBr_2$ to a cold (−78 °C) solution of **11** in THF. Thus, treatment of 2-cyclohexen-1-one (**23**) (see Chart I) with **12** in THF–Et_2O (−78 °C) in the presence of CuBr·Me_2S and BF_3·Et_2O,

(5) Piers, E.; Karunaratne, V. *Tetrahedron* **1989**, *45*, 1089.
(6) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(7) Kharasch, N.; Buess, C. M. *J. Am. Chem. Soc.* **1949**, *71*, 2724.
(8) Ashcroft, M. R.; Dass Gupta, B.; Johnson, M. D. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2021.
(9) Underwood, G. M.; Watts, C. T.; Kingsbury, C. A. *J. Org. Chem.* **1973**, *38*, 1553.

Table I. (*Z*)-Ethylidenecyclopentane Annulations



entry	enone[c]	conjugate addition product[c]	yield,[d] %	annulation product[c]	yield,[d] %
1	**23**	**30**	70	**37**	78
2	**24**	**31**	61	**38**	79
3	**25**	**32**[e]	64	**39**	83
4	**26**	**33**	69	**40**	78
5	**27**	**34**	57	**41**	86
6	**28**	**35**[f]	56	**42**	79
7	**29**	**36**	72	**43**	85

[a] The enone was treated (THF–Et_2O, −78 °C, 2 h) with 1 equiv of the Grignard reagent **12** in the presence of CuBr·Me_2S (0.3 equiv) and BF_2·Et_2O (1.2 equiv). [b] The chloro ketone was treated with 2.5 equiv of KH in THF (room temperature, 2.5 h). [c] See Chart I for structural formulas. [d] Yield of purified, distilled product. [e] This product consisted of a 2:1 mixture of diastereomers. [f] This product consisted of a 1:1 mixture of diastereomers.

followed by suitable workup and product purification, afforded the conjugate addition product **30** in 70% yield. In similar fashion, the enones **24–29** (Chart I) were converted into the corresponding chloro ketones **31–36**. The results of these experiments are summarized in Table I.

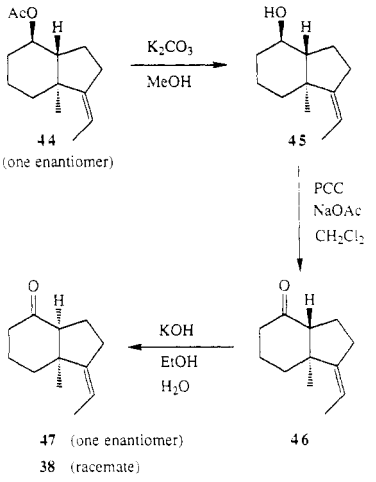
It is appropriate to note that the conjugate additions were generally more efficient when the solution of the Grignard reagent **12** in THF (−78 °C) was diluted with Et_2O prior to addition of CuBr·Me_2S, the enone, and BF_3·Et_2O. For example, conversion of **24** into **31** in THF alone proceeded in only 41% yield. Furthermore, the reaction efficiencies were also enhanced by use of BF_3·Et_2O, which is well known to promote conjugate additions of organocopper(I) reagents to α,β-unsaturated carbonyl systems.[10]

In some of the cases studied, the crude products contained small amounts of the corresponding enone starting materials. However, in each of these instances, the product was readily obtained in pure form by flash chromatography[6] of the mixture on silica gel. Not unexpectedly, the chloro ketones **32** and **35** (Table I, entries 3 and 6) consisted, in each case, of a mixture of epimers. Finally, it is well known that conjugate additions of cuprate reagents to bicyclo[3.3.0]oct-1-en-3-ones proceed in a highly stereoselective manner to provide cis-fused products.[11] Consequently, the stereochemistry of the chloro ketone **36** (entry 7) could be assigned with confidence.

Treatment of the conjugate addition products **30–36** with KH (2.5 equiv) in THF at room temperature provided, cleanly and efficiently, the corresponding (*Z*)-ethylidenecyclopentane annulation products **37–43** (Chart I, Table I). As judged by GLC and ^1H NMR analyses, all of the intramolecular alkylation products were stereochemically homogeneous.

On the basis of literature precedents[12] one would expect that cyclization of the chloro ketones **30–36** would provide initially (kinetic control) the corresponding cis-fused products **37–43**. Of these substances, **39** and **42** cannot undergo subsequent epimerization, since the chiral center adjacent to the carbonyl function is quaternary. Furthermore, trans-fused bicyclo[3.3.0]octane systems are much more strained (less stable) than their cis-fused counterparts, and, consequently, the initially produced products **40**, **41**, and **43** would not undergo epimerization. Therefore, at the outset, substances **37** and **38** were the only annulation products for which stereochemistry could not be assigned with certainty.

Scheme III



The relative configuration of the two chiral centers in **37** was determined as follows. In the ^1H NMR spectrum of this material, resonances at δ 2.62–2.70 (m), 3.00–3.06 (m), and 1.40 (dq, J = 4, 13 Hz) could be assigned, primarily on the basis of decoupling experiments, to protons H_A, H_B, and H_C, respectively. Thus, irradiation at δ 2.66 (H_A) simplified the multiplet at 3.00–3.06 (H_B) to a dd (J = 6, 13 Hz), while saturation of the signal at δ 3.03 (H_B) caused the resonances at 2.62–2.70 (H_A) and 1.40 (H_C) to change to a dd (J = 8, 9 Hz) and a dt (J = 4, 13 Hz), respectively. The size of the coupling constants associated with H_A and H_B, along with the fact that the signals due to these protons exhibit width-at-half-height values of 24 and 26 Hz, respectively, indicates that J_{AB} is about 7 Hz. This value, in turn, strongly suggests that **37** possesses a cis-fused ring junction. Verification of this conclusion was derived from a nuclear Overhauser enhancement (NOE) difference experiment. Thus, saturation of the signal at δ 3.03 (H_B) caused an enhancement of the resonance due to H_A (δ 2.62–2.70), clearly showing that H_A and H_B are in a cis relationship. Interestingly, signal enhancement was also observed for the resonance due to the vinyl methyl group (δ 1.64, dt, J = 7, 1.5 Hz). This result, along with the observed magnitude of the coupling constants associated with H_B and H_C (see above) reveals that **37** exists predominantly in the conformation **37A**. This conformational preference may be rationalized by noting that the alternative conformation **37B** is notably destabilized by a strong $A^{(1,3)}$ interaction[13] between the vinyl methyl group and H_C.

The stereochemistry of **38** was determined by means of a chemical correlation, as summarized in Scheme III. Hydrolysis of the olefinic acetate **44** (one enantiomer, absolute stereochemistry as shown),[14] followed by oxidation

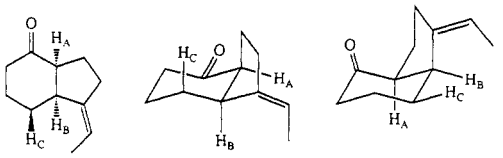
(10) Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 947. Lipshutz, B. H., Ellsworth, E. L.; Siahaan, T. J. *J. Am. Chem. Soc.* **1988**, *110*, 4834.

(11) Paquette, L. A.; Han, Y.-K. *J. Am. Chem. Soc.* **1981**, *103*, 1835. Paquette, L. A.; Annis, C. D. *Ibid.* **1983**, *105*, 7358. Paquette, L. A.; Roberts, R. A.; Drtina, G. J. *Ibid.* **1984**, *106*, 6690.

(12) Conia, J. M.; Rouessac, F. *Tetrahedron* **1961**, *16*, 45. Posner, G. H.; Sterling, J. J.; Whitten, C. E.; Lentz, C. M.; Brunelle, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 107.

(13) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

(14) Baggiolini, E. G.; Iacobelli, J. A.; Hennessy, B. M.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 2945. We are very grateful to Dr. Baggiolini for a generous sample of compound **44**.



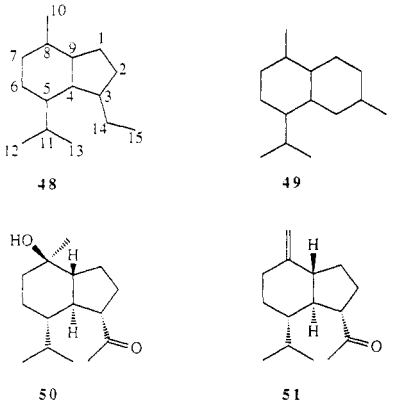
37 37A 37B

(pyridinium chlorochromate[15]) of the resultant alcohol, provided the ketone **46**. The spectra of this material were clearly different from those of the ketone **38** derived from ring closure of **31** (Table I, entry 2). However, treatment of **46** with KOH caused complete epimerization at the angular position adjacent to the carbonyl group and provided a product **47** that exhibited IR and ^1H NMR spectra identical with those of our (racemic) annulation product **38**. Thus, this bicyclic ketone also possesses a cis-fused ring junction.

The work outlined above showed that the Grignard reagent **12**, readily prepared from (*E*)-5-chloro-3-lithio-2-pentene (**11**), is a useful bifunctional reagent. In particular, reagent **12** can be used effectively to convert 2-cyclohexen-1-ones and 2-cyclopenten-1-ones into *cis*-7-[(*Z*)-ethylidene]bicyclo[4.3.0]nonan-2-ones and *cis*-6-[(*Z*)-ethylidene]bicyclo[3.3.0]octan-2-ones, respectively. Application of this new (*Z*)-ethylidenecyclopentane annulation method to the total synthesis of oplopanone-type sesquiterpenoids is described in the next section of this paper.

(c) Total Syntheses of (±)-Anhydrooplopanone (51), (±)-Oplopanone (50), and (±)-8-*epi*-Oplopanone (70). The oplopanane family of sesquiterpenoids is made up of a relatively small number of natural products that have the basic carbon skeleton **48** in common. From a structural viewpoint, the oplopananes are, formally, rearranged cadinanes, which possess the carbon skeleton **49**.

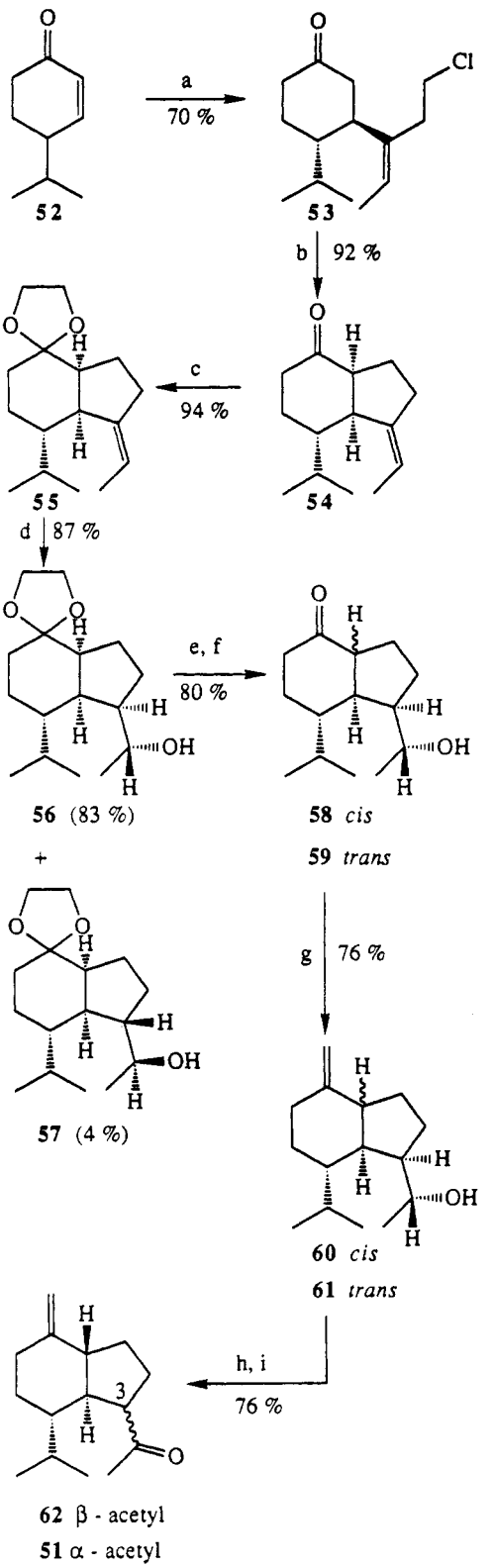
(−)-Oplopanone, the first member of the oplopanane family to be isolated and structurally characterized, was initially obtained from *Oplopanax japonicus*, a shrub that grows in the northern part of central Japan. On the basis of degradation, correlation, and optical rotatory dispersion studies, (−)-oplopanone was shown to possess the constitution and absolute stereochemistry depicted in structural formula **50**.[16] Subsequently, this substance was isolated



48 49 50 51

from a number of other terrestrial organisms.[17] Interestingly, (+)-oplopanone, the enantiomer of **50**, has been isolated from a marine source, the red alga *Laurencia subopposita*.[18] Prior to the work described below, two total syntheses of (±)-oplopanone (**50**) had been report-

Scheme IV[a]



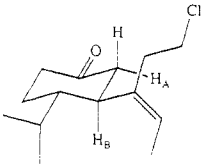
[a] (a) **12**, CuBr·Me_2S, BF_3·Et_2O, THF–Et_2O, −78 °C, 2 h; (b) KH, THF; (c) $HOCH_2CH_2OH$, C_5H_5N·*p*-TsOH, PhH; (d) BH_3·Me_2S, THF, H_2O_2, NaOH, H_2O, 40–50 °C; (e) C_5H_5N·*p*-TsOH, acetone–H_2O; (f) NaOMe, MeOH; (g) $Ph_3P{=}CH_2$, DMSO; (h) C_5H_5N·CrO_3·HCl, NaOAc, CH_2Cl_2; (i) NaOMe, MeOH, 60 °C.

(15) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(16) Takeda, K.; Minato, H.; Ishikawa, M. *Chem. Commun.* **1965**, 79; *Tetrahedron, Suppl. No. 7* **1966**, 219.
(17) (a) Babkin, V. A.; Dubovenko, Zh, V.; Pentegova, V. A. *Izv. Sib. Otd. Akad. Nauk SSSR. Ser. Khim Nauk* **1970**, 168. (b) Rowe, J. W.; Ronald, R. C.; Nagasampagi, B. A. *Phytochemistry* **1972**, *11*, 365.
(18) Wratten, S. J.; Faulkner, D. J. *J. Org. Chem.* **1977**, *42*, 3343.

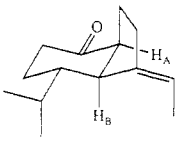
ed.[19,20] A biomimetic synthesis of **50** from germacrene D has also been described.[21]

The keto alkene (−)-anhydrooplopanone (**51**) has been isolated from *Euryops pedunculatus*[22] and *Rugelia nudicaulis*.[23] Dehydration of (−)-oplopanone (**50**) affords **51**, along with a double-bond isomer.[17a]

A concise synthesis of (±)-anhydrooplopanone (**51**) via a route in which the newly developed (*Z*)-ethylidenecyclopentane annulation method played a key role, is outlined in Scheme IV. Conjugate addition of the Grignard reagent **12** to commercially available 4-isopropyl-2-cyclohexen-1-one (**52**) provided, highly stereoselectively, the chloro ketone **53**. The expectation that the reagent would add to the enone from the side opposite to the isopropyl group was corroborated by the ^{1}H NMR spectrum of the product **53**. In particular, the protons H_A and H_B (see **53A**) appear as a ddd (J = 2.5, 4.5, 13 Hz) and a dt (J = 4.5, 12 Hz) at δ 2.17 and 2.89, respectively. In a decoupling experiment, irradiation at δ 2.17 (H_A) modified the signal at 2.89 (H_B) to a t (J = 12 Hz), thus showing that J_{AB} = 4.5 Hz. The magnitude of the other coupling constants associated with the H_B signal (12 Hz) demonstrates that this proton is axially oriented and is vicinal to two other axial protons. These observations are consistent only with the conclusions that, in **53**, the two substituents are in a trans relationship and that, as expected, this substance prefers the conformation shown in **53A**.



53A



54A

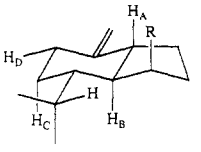
Intramolecular alkylation of **53** provided a single product **54**, the stereochemistry of which remains unaltered when this substance is treated with *t*-BuOK in *t*-BuOH at 35–40 °C for 15 h. The stereochemistry of **54** was, again, demonstrated by ^{1}H NMR spectroscopy. In the spectrum of **54**, the angular protons H_A and H_B (see **54A**) produce a broad q (J = 7 Hz) and a broad dd (J = 7, 10 Hz) at δ 2.63 and 2.88, respectively. Irradiation at δ 2.88 (H_B) changed the signal at 2.63 (H_A) to a broad t (J = 7 Hz), while saturation of the δ 2.63 resonance (H_A) simplified the broad dd at 2.88 (H_B) to a broad d (J = 10 Hz). Thus, J_{AB} = 7 Hz. Furthermore, in a NOE difference experiment, irradiation at δ 2.88 (H_B) caused signal enhancement at 2.63 (H_A) and 1.63 (the resonance due to the vinyl methyl group). On the basis of these data, one can conclude with confidence that the annulation product **54** has a cis-fused ring junction and exists (largely) in the conformation **54A**.

Hydroboration of the ketal alkene **55**, which was readily derived from the corresponding ketone **54**, provided a chromatographically separable mixture of two products, in a ratio of 95:5. Since one would expect the borane reagent to approach the double bond in **55** from the more open convex face of the molecule, the major and minor products were assigned structures **56** and **57**, respectively.

Treatment of **56** with pyridinium *p*-toluenesulfonate in refluxing aqueous acetone gave a 1:2 mixture of two keto alcohols. Clearly, partial epimerization at the angular carbon adjacent to the carbonyl group had occurred during the hydrolysis reaction. When the product composition during the hydrolysis process was carefully monitored, it became apparent that the cis-fused ketone **58**, the initially formed hydrolysis product, is the less stable isomer, while the more stable epimer is the subsequently produced, trans-fused ketone **59**. Indeed, treatment of the 1:2 mixture of **58** and **59** with NaOMe in MeOH produced a 1:3 (equilibrium) mixture of these two substances. This ratio did not change with longer reaction times.

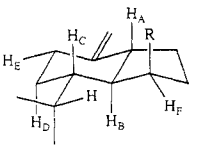
Reaction of the 1:3 mixture of **58** and **59** with 3 equiv of $Ph_3P{=}CH_2$ in dimethyl sulfoxide (DMSO),[24] followed by chromatographic separation of the resultant product mixture, afforded the olefinic alcohols **60** and **61**, in isolated yields of 4% and 76%, respectively. Evidently, under the reaction conditions, relatively rapid equilibration of **58** and **59** occurred and, importantly, the rate of the Wittig reaction of the trans isomer **59** (to produce **61**) was greater than that associated with the conversion of the cis isomer **58** into **60**. Consequently, even though, from a synthetic viewpoint, the equilibrium ratio of the ketones **58** and **59** was not particularly encouraging, the Wittig process produced the desired trans-fused alkene **61** with high stereoselectivity and in very good yield.[25]

In the ^{1}H NMR spectrum of the major Wittig product **61**, the protons H_B and H_C (see **61A**) give rise to a dt (J = 8, 11 Hz) and a dq (J = 4, 11 Hz) at δ 1.20 and 1.05, respectively. Furthermore, the allylic protons H_A and H_D exhibit an overlapped m at δ 2.30–2.39. In a decoupling experiment, irradiation at δ 2.35 (H_A + H_D) modified the signals at δ 1.20 (H_B) and 1.05 (H_C) to a dd (J = 8, 11 Hz) and a q (J = 11 Hz), respectively. Thus, J_{AB} = 11 Hz, and one can therefore conclude that the major Wittig product does indeed possess a trans-fused ring junction.



61A R = CH(OH)Me

Oxidation[15] of the olefinic alcohol **61** provided (±)-3-*epi*-anhydrooplopanone (**62**). ^{1}H NMR spectroscopy unequivocally established the relative stereochemistry at each of the chiral centers in **62**. The chemical shifts, multiplicities, and coupling constants of a number of assignable resonances are shown in conjunction with the conformational formula **62A**. Decoupling experiments corroborated



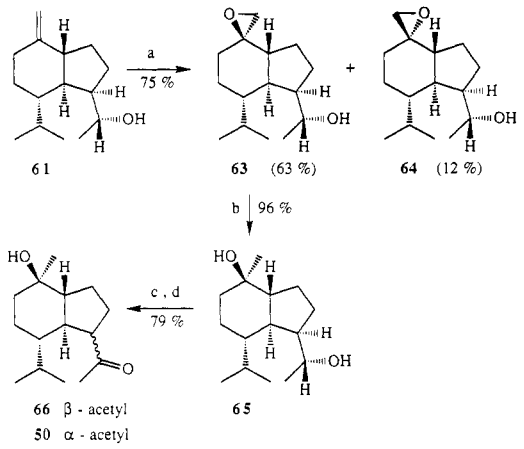
62A R = Ac

H_A 2.46 - 2.57 (m)
H_B 1.27 (dt, J = 7, 12 Hz)
H_C 1.81 (tt, J = 3, 12 Hz)
H_D 0.98 (dq, J = 4, 12 Hz)
H_E 2.33 (td, J = 4, 13 Hz)
H_F 3.15 (ddd, J = 4, 7, 9 Hz)

these assignments and showed that J_{AB} = J_{BC} = 12 Hz. Consequently, each of these protons (H_A, H_B, H_C) must

(19) Caine, D.; Tuller, F. N. *J. Am. Chem. Soc.* **1971**, *93*, 6311; *J. Org. Chem.* **1973**, *38*, 3663.
(20) Taber, D. F.; Korsmeyer, R. W. *J. Org. Chem.* **1978**, *43*, 4925.
(21) Shizuri, Y.; Yamaguchi, S.; Terada, Y.; Yamamura, S. *Tetrahedron Lett.* **1986**, *27*, 57.
(22) Bohlmann, F.; Zdero, C. *Phytochemistry* **1978**, *17*, 1135.
(23) Bohlmann, F.; Gupta, R. K.; Jakupovic, J.; King, R. M.; Robinson, H. *Phytochemistry* **1982**, *21*, 1665.
(24) Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128.
(25) Overall processes involving equilibration of epimeric substrate ketones, in conjunction with Wittig reactions that proceed with significantly different rates, have been observed previously. See, for example: Marshall, J. A.; Pike, M. T.; Carroll, R. D. *J. Org. Chem.* **1966**, *31*, 2933. Heathcock, C. H.; Ratcliffe, R. *J. Am. Chem. Soc.* **1971**, *93*, 1746.

Scheme V[a]

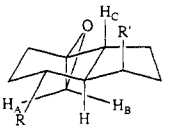


[a] (a) NBS, H_2O–DMSO, K_2CO_3, MeOH; (b) $LiAlH_4$, Et_2O; (c) $C_5H_5N{\cdot}CrO_3{\cdot}HCl$, NaOAc, CH_2Cl_2; (d) NaOMe, MeOH, 40–45 °C.

have an axial orientation on the six-membered ring. In a NOE difference experiment, saturation of the signal at δ 1.27 (H_B) caused enhancement of the resonance at 3.15 (H_F), thus establishing a cis relationship between these two protons.

Base-catalyzed equilibration of the ketone **62** produced a 7:93 mixture of **62** and (±)-anhydrooplopanone (**51**). Fractional crystallization of this mixture from petroleum ether provided pure (±)-**51**, mp 68 °C, which exhibited a ^1H NMR spectrum identical with that of (−)-anhydrooplopanone.[26] Furthermore, the IR and ^{13}C NMR spectral data obtained from our synthetic material agreed well with those reported for the natural product.[22]

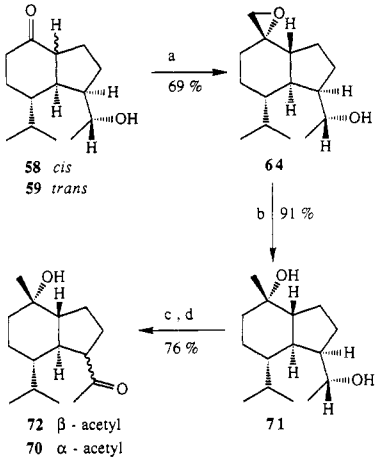
A total synthesis of (±)-oplopanone (**50**), starting from the previously prepared olefinic alcohol **61** (vide supra), is summarized in Scheme V. Reaction of **61** with *N*-bromosuccinimide in aqueous dimethyl sulfoxide[27] gave a mixture of bromohydrins, which, when treated with K_2CO_3 in MeOH, afforded a mixture of two epoxides in a ratio of about 5:1. Flash chromatography[6] of this material provided the pure, epimeric substances **63** (63%) and **64** (12%). In the ^1H NMR spectrum of the major epoxide **63**, the signals due to the protons H_A and H_B (see conformational formula **63A**) appear at δ 2.86 (dd, J = 2, 5



63A R = *i* - Pr
R' = CH(OH)Me

Hz) and 2.48 (d, J = 5 Hz), respectively. The small coupling constant (2 Hz) associated with the former resonance can be attributed to a long-range W-type coupling[28] between H_A and the angular proton H_C. Molecular models indicate that W-type coupling between H_C and one of the protons on the methylene carbon associated with the oxirane ring is possibly only if the epoxide possesses the stereochemistry shown in **63**. Indeed, in the ^1H NMR spectrum of the epimeric epoxide **64**, the protons on the oxirane methylene carbon give rise to simple doublets (J = 5 Hz) at δ 2.57 and 2.66. These data provided good evidence for the stereochemical assignments.

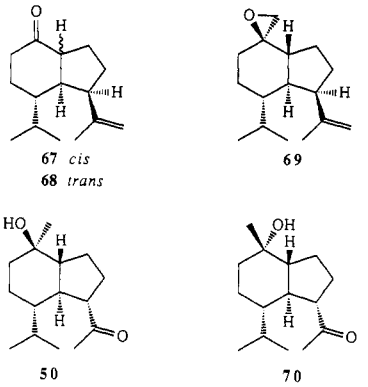
Scheme VI[a]



[a] (a) $Me_2S{=}CH_2$, DMSO–THF; (b) $LiAlH_4$, Et_2O; (c) $C_5H_5N{\cdot}CrO_3{\cdot}HCl$, NaOAc, CH_2Cl_2; (d) NaOMe, MeOH, 60 °C.

Reduction of the epoxy alcohol **63** provided the nicely crystalline diol **65**, which, upon oxidation, gave (±)-3-*epi*-oplopanone (**66**). Equilibration of this ketone with NaOMe in MeOH produced a 6:94 mixture of **66** and (±)-oplopanone (**50**). Pure (±)-**50**, derived by fractional crystallization of this material from hexane–diethyl ether, exhibited spectra identical with those of (−)-oplopanone[29] and of previously synthesized (±)-**50**.[20,29] Furthermore, the melting point of our synthetic material (99–100 °C) was very similar to those reported (101.5–102 °C,[19] 97–98 °C[20]) previously for (±)-**50**.

In 1981, Köster and Wolf reported[30] an efficient synthesis of a 2:3 mixture of the bicyclic ketones **67** and **68**. Treatment of this mixture with dimethylsulfonium methylide[31] under conditions that would be expected to equilibrate the epimeric starting materials was reported[30] to give primarily the epoxide **69**. Subjection of this substance to an appropriate sequence of reactions (reduction with $LiAlH_4$, ozonolysis, and base-promoted equilibration) was claimed[30] to provide (±)-oplopanone (**50**). However,



the melting point (63–64 °C) of the synthetic substance obtained is very different from those of samples of (±)-**50** prepared in other laboratories (vide supra). Consequently, it appeared that Köster and Wolf[30] had prepared not (±)-oplopanone (**50**), but an isomeric substance, most likely

(26) We thank Professor F. Bohlmann for a copy of the ^1H NMR spectrum of (−)-**51**.
(27) Yamazaki, M.; Shibasaki, M.; Ikegami, I. *Chem. Lett.* **1981**, 1245.
(28) Jackman, L. M.; Sternhell, S. In *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon Press: New York, 1969; pp 222, 234.
(29) We are grateful to Dr. M. Matsumoto, Shionogi Research Laboratory, for a sample of (−)-**50** and for copies of its IR and ^1H NMR spectra, and to Professor Taber for copies of the IR, ^1H NMR, and mass spectra of (±)-**50**.
(30) Köster, F.-H.; Wolf, H. *Tetrahedron Lett.* **1981**, *22*, 3937.

(±)-8-*epi*-oplopanone (**70**). In order to test this conjecture, the reaction sequence summarized in Scheme VI was carried out.

Treatment of the previously synthesized 1:3 mixture of the ketols **58** and **59** (vide supra) with an excess of dimethylsulfonium methylide[31] in DMSO–THF (equilibration conditions) gave, after flash chromatography[6] of the crude product, the crystalline epoxide **64** (69%). This material exhibited melting point and spectra identical with those of the minor epoxide **64** obtained from the olefinic alcohol **61** (vide supra, Scheme V). Reduction of **64**, followed by oxidation of the resultant diol **71**, provided (±)-3,8-di-*epi*-oplopanone (**72**). Base-catalyzed equilibration of **72** afforded a 7:93 mixture of **72** and (±)-8-*epi*-oplopanone (**70**). Pure (±)-**70**, obtained from this mixture by flash chromatography[6] and recrystallization, exhibited a 400-MHz ^{1}H NMR spectrum very similar to, but clearly different from, that of (±)-oplopanone. Furthermore, the melting point (62 °C) of our synthetic (±)-**70** was distinctly different from that of racemic oplopanone (**50**) but very similar to that (63–64 °C) of the synthetic material obtained by Köster and Wolf.[30] Consequently, it is highly probable that these workers had synthesized (±)-8-*epi*-oplopanone (**70**) and not, as they had thought, (±)-oplopanone (**50**).

Experimental Section[32]

(*E*)-3-Trimethylstannyl-3-penten-1-ol (17). To a cold (−20 °C), stirred solution of $LiAlH_4$ (247 mg, 6.5 mmol) in 50 mL of dry Et_2O (argon atmosphere) was added a solution of ethyl (*E*)-3-trimethylstannyl-3-pentenoate (**9**) (2.91 g, 10 mmol) in 10 mL of dry Et_2O. After the mixture had been stirred at −20 °C for 1.5 h, $Na_2SO_4 \cdot 10H_2O$ was added in portions to destroy the excess reducing agent. The resulting slurry was filtered through a short column of Florisil (30 g) and the column was eluted with Et_2O. Concentration of the eluate and distillation (75–90 °C (0.3 Torr)) of the residual liquid gave 2.16 g (87%) of the alcohol **17**, a colorless oil: IR (neat) 3300, 1600, 1040, 770 cm^{-1}; ^{1}H NMR (80 MHz) δ 0.13 (s, 9 H, $^2J_{Sn-H}$ = 52 Hz), 1.45 (t, 1 H, *J* = 7 Hz, exchanges with D_2O), 1.75 (d, 3 H, *J* = 7 Hz), 2.58 (t, 2 H, *J* = 7 Hz), 3.62 (q, 2 H, *J* = 7 Hz), 5.87 (tq, 1 H, *J* = 2.5, 7 Hz, $^3J_{Sn-H}$ = 77 Hz); exact mass calcd for $C_7H_{15}OSn$ (M^+ − Me) 235.0144, found 235.0156.

(*Z*)-3-Trimethylstannyl-3-penten-1-ol (14). A procedure identical with that described above was employed. From 2.91 g of ethyl (*Z*)-3-trimethylstannyl-3-pentenoate (**7**) there was obtained 2.18 g (88%) of the alcohol **14**, distillation temperature 60–75 °C (0.2 Torr): IR (neat) 3300, 1600, 1040, 770 cm^{-1}; ^{1}H NMR (80 MHz) δ 0.23 (s, 9 H, $^2J_{Sn-H}$ = 52 Hz), 1.60 (br s, 1 H, exchanges with D_2O), 1.77 (br d, 3 H, *J* = 7 Hz), 2.48 (br t, 2 H, *J* = 7 Hz), 3.56 (t after addition of D_2O, 2 H, *J* = 7 Hz), 6.20 (tq, 1 H, *J* = 2.5, 7 Hz, $^3J_{Sn-H}$ = 138 Hz); exact mass calcd for $C_7H_{15}OSn$ (M^+ − Me) 235.0144, found 235.0146.

(*E*)-5-Chloro-3-trimethylstannyl-2-pentene (10). To a stirred solution of the alcohol **17** (1.245 g, 5 mmol) in 30 mL of dry CCl_4 (argon atmosphere) were added dry Et_3N (765 μL, 5.5 mmol) and Ph_3P (2.62 g, 10 mmol), and the resulting mixture was refluxed for 24 h. The solution was cooled, petroleum ether (50 mL) was added, and the resulting slurry was filtered through a column of Florisil (25 g, elution with petroleum ether). Concentration of the eluate, followed by distillation (40–55 °C (0.3 Torr)) of the remaining material, provided 1.013 g (76%) of the chloride **10**, a colorless oil: IR (neat) 1600, 770, 740 cm^{-1}; ^{1}H NMR (80 MHz) δ 0.18 (s, 9 H, $^2J_{Sn-H}$ = 52 Hz), 1.75 (d, 3 H, *J* = 7 Hz), 2.75 (br t, 2 H, *J* = 7 Hz), 3.45 (t, 2 H, *J* = 7 Hz), 5.83 (tq, 1 H, *J* = 2, 7 Hz, $^3J_{Sn-H}$ = 76 Hz); exact mass calcd for $C_7H_{14}{}^{35}ClSn$ (M^+ − Me) 252.9806, found 252.9814.

(*Z*)-5-Chloro-3-trimethylstannyl-2-pentene (8). A procedure similar to that described above was employed. From 2.49 g (10 mmol) of the alcohol **14** there was obtained 2.21 g (83%) of the chloride **8**, distillation temperature 40–50 °C (0.3 Torr): IR (neat) 1610, 770, 740 cm^{-1}; ^{1}H NMR (80 MHz) δ 0.20 (s, 9 H, $^2J_{Sn-H}$ = 52 Hz), 1.75 (br d, 3 H, *J* = 7 Hz), 2.60 (br t, 2 H, *J* = 7 Hz), 3.45 (t, 2 H, *J* = 7 Hz), 6.20 (tq, 1 H, *J* = 2, 7 Hz, $^3J_{Sn-H}$ = 135 Hz); exact mass calcd for $C_7H_{14}{}^{35}ClSn$ (M^+ − Me) 252.9806, found 252.9807.

Transmetalation of (*E*)-5-Chloro-3-trimethylstannyl-2-pentene (10). Trapping of Ethylidenecyclopropane (18) with 2,4-Dinitrobenzenesulfenyl Chloride (19). To a cold (−78 °C), stirred solution of the chloro stannane **10** (200 mg, 0.75 mmol) in 2 mL of dry THF (argon atmosphere) was added a solution of MeLi in Et_2O (0.57 mL, 0.82 mmol). After the light yellow solution had been stirred at −78 °C for 20 min, a solution of 2,4-dinitrobenzenesulfenyl chloride (**19**) (160 mg, 0.91 mmol) in 4 mL of dry CH_2Cl_2 was added; the mixture was allowed to warm slowly to room temperature and then was stirred for 16 h. Removal of the solvent, followed by flash chromatography of the residual material on silica gel (18 g, elution with 85:15 petroleum ether–ethyl acetate), gave a yellow solid. Recrystallization of this material from hexane–acetone produced 111 mg (54%) of 1-(1-chloroethyl)-1-(2,4-dinitrophenylthio)cyclopropane (**20**), mp 128–130 °C: IR (KBr) 3050, 1570, 1500, 1330, 1040, 910, 830, 730 cm^{-1}; ^{1}H NMR (80 MHz, $(CD_3)_2CO$) δ 1.20–1.40 (m, 3 H), 1.52–1.65 (m, 1 H), 1.66 (d, 3 H, *J* = 7 Hz), 4.38 (q, 1 H, *J* = 7 Hz), 8.40 (d, 1 H, *J* = 10 Hz), 8.54 (dd, 1 H, *J* = 2, 10 Hz), 8.98 (d, 1 H, *J* = 2 Hz); exact mass calcd for $C_{11}H_{11}N_2O_4{}^{35}ClS$ 302.0129, found 302.0123.

Transmetalation of (*Z*)-5-Chloro-3-trimethylstannyl-2-pentene (8). Preparation of (*Z*)-5-Chloro-3-(1-hydroxycyclohexyl)-2-pentene (15) and (*Z*)-4-Ethylidene-1-oxaspiro[4.5]undecane (16). To a cold (−78 °C), stirred solution of the chloro stannane **8** (134 mg, 0.5 mmol) in 2 mL of dry THF (argon atmosphere) was added a solution of MeLi in Et_2O (0.43 mL, 0.55 mmol), and the resultant light yellow solution was stirred at −78 °C for 20 min. Cyclohexanone (57 μL, 0.55 mmol) was added and stirring was continued for 45 min. Saturated aqueous NH_4Cl (0.5 mL) and Et_2O (10 mL) were added and the mixture was warmed to room temperature. The phases were separated and the aqueous layer was washed with Et_2O. The combined organic extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. Flash chromatography of the residual material on silica gel (10 g, elution with 93:7 petroleum ether–Et_2O) gave 33 mg (40%) of the spiro ether **16** and 31 mg (31%) of the chloro alcohol **15**.

Compound **16** (distillation temperature 40–55 °C (0.2 Torr)) exhibited IR (neat) 1060, 910 cm^{-1}; ^{1}H NMR (80 MHz) δ 1.18–1.80 (diffuse m, 13 H), 2.35–2.68 (m, 2 H), 3.75 (t, 2 H, *J* = 7 Hz), 5.36 (tq, 1 H, *J* = 2, 7 Hz); exact mass calcd for $C_{11}H_{18}O$ 166.1358, found 166.1359.

The chloro alcohol **15** (distillation temperature 70–85 °C (0.2 Torr)) exhibited IR (neat) 3425, 1120, 960 cm^{-1}; ^{1}H NMR (80 MHz) δ 1.05–2.20 (diffuse m, 14 H), 2.48 (br t, 2 H, *J* = 7 Hz), 3.60 (t, 2 H, *J* = 7 Hz), 5.36 (tq, 1 H, *J* = 1, 7 Hz); exact mass calcd for $C_{11}H_{19}{}^{35}ClO$ 202.1126, found 202.1126.

General Procedure A: Copper(I)-Catalyzed Conjugate Addition of the Grignard Reagent 12 to Enones. A solution of MeLi in Et_2O (0.45 mL, 0.55 mmol) was added to a cold (−78 °C), stirred solution of the chloro stannane **8** (134 mg, 0.5 mmol) in 2 mL of dry THF (argon atmosphere). After the solution had been stirred at −78 °C for 20 min, anhydrous $MgBr_2$ (110 mg, 0.6 mmol) was added and the resultant milky solution was stirred for 10 min. The solution was diluted by dropwise addition of dry Et_2O (4 mL), and stirring was continued at −78 °C for 10 min. After successive addition of $CuBr \cdot Me_2S$ (31 mg, 0.15 mmol), the enone (0.5 mmol), and $BF_3 \cdot Et_2O$ (75 μL, 0.6 mmol), the yellow solution was stirred at −78 °C for 2 h. Saturated aqueous NH_4Cl–NH_4OH (pH 8) (3 mL) and Et_2O (10 mL) were added and the mixture was warmed to room temperature. Vigorous stirring was maintained with exposure to air until the aqueous phase became deep blue. The phases were separated and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. The remaining oil, upon purification by flash chromatography on silica gel (10 g, elution with 3:1 petroleum ether–Et_2O) and distillation, provided the conjugate addition product.

(31) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.
(32) For general procedures, see ref 1.

The following substances were prepared via this general procedure.

3-[(*Z*)-3-(5-Chloro-2-pentenyl)]cyclohexanone (30): 71 mg (70%), from 48 mg (0.5 mmol) of 2-cyclohexen-1-one (**23**); distillation temperature 75–90 °C (0.2 Torr); IR (neat) 1710, 1230, 885, 740 cm^{-1}; ^1H NMR (400 MHz) δ 1.63 (br d, 3 H, J = 7 Hz), 1.67–1.79 (m, 3 H), 2.10–2.53 (m, 7 H), 2.88–2.98 (m, 1 H), 3.50–3.63 (m, 2 H), 5.32 (q, 1 H, J = 7 Hz); exact mass calcd for $C_{11}H_{17}{}^{35}ClO$ 200.0969, found 200.0966.

3-[(*Z*)-3-(5-Chloro-2-pentenyl)]-3-methylcyclohexanone (31): 65 mg (61%) from 55 mg (0.5 mmol) of 3-methyl-2-cyclohexen-1-one (**24**); distillation temperature 90–105 °C (0.2 Torr); IR (neat) 1705, 1230, 740 cm^{-1}; ^1H NMR (400 MHz) δ 1.19 (s, 3 H), 1.72–1.78 (m, 1 H), 1.79 (d, 3 H, J = 7 Hz), 1.83–1.92 (m, 2 H), 2.07–2.16 (m, 1 H), 2.26–2.35 (m, 3 H), 2.39–2.53 (m, 2 H), 2.68 (d, 1 H, J = 14 Hz), 3.47–3.57 (m, 2 H), 5.38 (q, 1 H, J = 7 Hz). Decoupling experiment: irradiation at δ 3.52 simplified the multiplet at δ 2.39–2.53 to a pair of doublets (J = 14 Hz in each case); exact mass calcd for $C_{12}H_{19}{}^{35}ClO$ 214.1126, found 214.1125.

3-[(*Z*)-3-(5-Chloro-2-pentenyl)]-2-methylcyclohexanone (32): 68 mg (64%) from 55 mg (0.5 mmol) of 2-methyl-2-cyclohexen-1-one (**25**); distillation temperature 105–120 °C (0.3 Torr); IR (neat) 1700, 1230, 730 cm^{-1}. On the basis of its ^1H NMR spectrum (400 MHz), this material consisted of a 2:1 mixture of epimers: δ 0.90, 1.06 (d, d, ratio 2:1, 3 H, J = 7 Hz in each case), 1.55–2.66 (m, 12 H), 3.02–3.12 (m, 1 H), 3.49–3.70 (m, 2 H), 5.32–5.48 (m, 1 H); exact mass calcd for $C_{12}H_{19}{}^{35}ClO$ 214.1126, found 214.1127.

3-[(*Z*)-3-(5-Chloro-2-pentenyl)]cyclopentanone (33): 64 mg (69%) from 41 mg (0.5 mmol) of 2-cyclopenten-1-one (**26**); distillation temperature 85–100 °C (0.3 Torr); IR (neat) 1730, 1160, 740 cm^{-1}; ^1H NMR (400 MHz) δ 1.69 (br d, 3 H, J = 7 Hz), 1.72–1.85 (m, 1 H), 2.01–2.50 (m, 7 H), 3.25–3.35 (m, 1 H), 3.50–3.59 (m, 2 H), 5.42 (q, 1 H, J = 7 Hz); exact mass calcd for $C_{10}H_{15}{}^{35}ClO$ 186.0813, found 186.0816.

3-[(*Z*)-3-(5-Chloro-2-pentenyl)]-3-methylcyclopentanone (34): 57 mg (57%) from 47 mg (0.5 mmol) of 3-methyl-2-cyclopenten-1-one (**27**); distillation temperature 85–95 °C (0.2 Torr); IR (neat) 1730, 1165, 745 cm^{-1}; ^1H NMR (400 MHz) δ 1.22 (s, 3 H), 1.73 (d, 3 H, J = 7 Hz), 2.11–2.18 (m, 2 H), 2.25–2.33 (m, 2 H), 2.45 (s, 2 H), 2.48–2.55 (m, 2 H), 3.57 (t, 2 H, J = 7 Hz), 5.34 (q, 1 H, J = 7 Hz); exact mass calcd for $C_{11}H_{17}{}^{35}ClO$ 200.0969, found 200.0966.

3-[(*Z*)-3-(5-Chloro-2-pentenyl)]-2-methylcyclopentanone (35): 56 mg (56%) from 47 mg (0.5 mmol) of 2-methyl-2-cyclopenten-1-one (**28**); distillation temperature 90–100 °C (0.2 Torr); IR (neat) 1725, 1155, 735 cm^{-1}. On the basis of its ^1H NMR spectrum (400 MHz), this material consisted of a 1:1 mixture of epimers: δ 0.92, 1.00 (d, d, ratio 1:1, 3 H, J = 7 Hz in each case), 1.65, 1.68 (d, d, ratio 1:1, 3 H, J = 7 Hz in each case), 1.70–2.49 (m, 7 H), 2.85, 3.45 (dt, q, ratio 1:1, 1 H, J = 6, 11 Hz and 8 Hz, respectively), 3.50–3.63 (m, 2 H), 5.45, 5.52 (q, q, ratio 1:1, 1 H, J = 7 Hz in each case); exact mass calcd for $C_{11}H_{17}{}^{35}ClO$ 200.0969, found 200.0963.

***cis*-1-[(*Z*)-3-(5-Chloro-2-pentenyl)]bicyclo[3.3.0]octan-3-one (36)**: 81 mg (72%) from 61 mg (0.5 mmol) of bicyclo[3.3.0]oct-1-en-3-one (**29**); distillation temperature 115–130 °C (0.3 Torr); IR (neat) 1725, 1170, 745 cm^{-1}; ^1H NMR (400 MHz) δ 1.43–1.58 (m, 3 H), 1.69 (d, 3 H, J = 7 Hz), 1.65–1.78 (m, 1 H), 1.92–2.04 (m, 3 H), 2.10 (dd, 1 H, J = 5, 18 Hz), 2.46–2.59 (m, 4 H), 2.84–2.91 (m, 1 H), 3.46–3.57 (m, 2 H), 5.36 (q, 1 H, J = 7 Hz); exact mass calcd for $C_{13}H_{19}{}^{35}ClO$ 226.1126, found 226.1121.

***trans*-3-[(*Z*)-3-(5-Chloro-2-pentenyl)]-4-isopropylcyclohexanone (53)**: 845 mg (70%) from 690 mg (5.0 mmol) of 4-isopropyl-2-cyclohexen-1-one (**52**). The crude product was not chromatographed, but was distilled (140–155 °C (0.3 Torr)) directly: IR (neat) 1710, 1200, 730 cm^{-1}; ^1H NMR (400 MHz) δ 0.72, 0.96 (d, d, 3 H each, J = 7 Hz in each case), 1.44 (dq, 1 H, J = 4.5, 13 Hz), 1.64 (dt, 3 H, J = 7, 1.5 Hz), 1.67–1.78 (m, 2 H), 1.98–2.05 (m, 1 H), 2.17 (ddd, 1 H, J = 2.5, 4.5, 13 Hz), 2.30–2.49 (m, 5 H), 2.89 (dt, 1 H, J = 4.5, 12 Hz), 3.55–3.65 (m, 2 H), 5.36 (q, 1 H, J = 7 Hz). Decoupling experiment: irradiation at δ 2.17 changed the signal at δ 2.89 to a t (J = 12 Hz) and sharpened the multiplets at δ 2.30–2.49 and 1.98–2.05; exact mass calcd for $C_{14}H_{23}{}^{35}ClO$ 242.1449, found 242.1444.

General Procedure B: Preparation of (*Z*)-Ethylidenecyclopentane Annulation Products. To a stirred suspension of KH (30 mg, 0.75 mmol) in 2 mL of dry THF (argon atmosphere) was added, dropwise, a solution of the appropriate chloro ketone (0.3 mmol) in 1 mL of dry THF. The yellow mixture was stirred at room temperature for 2.5 h. Saturated aqueous NH_4Cl (3 mL) and Et_2O (8 mL) were added and the mixture was stirred for 10 min. The phases were separated and the aqueous layer was washed thoroughly with Et_2O. The combined organic extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. Distillation of the residual oil provided the annulation product.

The following substances were prepared via this general procedure.

***cis*-7-[(*Z*)-Ethylidene]bicyclo[4.3.0]nonan-2-one (37)**: 38 mg (78%) from 60 mg (0.3 mmol) of the chloro ketone **30**; distillation temperature (45–60 °C (0.2 Torr); IR (neat) 1700, 1230, 890 cm^{-1}; ^1H NMR (400 MHz) δ 1.40 (dq, 1 H, J = 4, 13 Hz), 1.64 (dt, 3 H, J = 7, 1.5 Hz), 1.72 (ddq, 1 H, J = 4, 5, 13 Hz), 1.83–2.05 (m, 4 H), 2.25–2.55 (m, 4 H), 2.62–2.70 (m, 1 H), 3.00–3.06 (m, 1 H), 5.29 (tq, 1 H, J = 2, 7 Hz). Decoupling experiments: irradiation at δ 2.66 caused simplification of the signal at 3.00–3.06 to a dd (J = 6, 13 Hz) and sharpened the signal at 1.83–2.05, while irradiation at δ 3.03 changed the resonances at 2.62–2.70 and 1.40 to a dd (J = 8, 9 Hz) and a dt (J = 4, 13 Hz), respectively, and sharpened the multiplet at 1.83–2.05. NOE difference experiment: irradiation at δ 3.03 caused signal enhancement at 2.66 and 1.64; exact mass calcd for $C_{11}H_{16}O$ 164.1202, found 164.1196.

***cis*-7-[(*Z*)-Ethylidene]-6-methylbicyclo[4.3.0]nonan-2-one (38)**: 42 mg (79%) from 64 mg (0.3 mmol) of the chloro ketone **31**; distillation temperature 45–60 °C (0.2 Torr); IR (neat) 1700, 1240 cm^{-1}; ^1H NMR (400 MHz) δ 1.32 (s, 3 H), 1.67 (dt, 3 H, J = 7, 2 Hz), 1.70–1.79 (m, 2 H), 1.83–2.05 (m, 4 H), 2.25–2.32 (m, 1 H), 2.36–2.45 (m, 4 H), 5.28 (tq, 1 H, J = 2, 7 Hz); exact mass calcd for $C_{12}H_{18}O$ 178.1358, found 178.1358.

***cis*-7-[(*Z*)-Ethylidene]-1-methylbicyclo[4.3.0]nonan-2-one (39)**: 44 mg (83%) from 64 mg (0.3 mmol) of the chloro ketone **32**; distillation temperature 45–60 °C (0.2 Torr); IR (neat) 1710, 1440 cm^{-1}; ^1H NMR (400 MHz) δ 1.06 (s, 3 H), 1.40–1.50 (m, 2 H), 1.64 (dt, 3 H, J = 7, 2 Hz), 1.71 (tq, 1 H, J = 5, 12 Hz), 1.80–1.88 (m, 1 H), 1.92–2.00 (m, 1 H), 2.09–2.17 (m, 1 H), 2.31–2.42 (m, 2 H), 2.43–2.54 (m, 2 H), 2.63 (dd, 1 H, J = 5, 12 Hz), 5.29 (tq, 1 H, J = 2, 7 Hz); exact mass calcd for $C_{12}H_{18}O$ 178.1358, found 178.1359.

***cis*-6-[(*Z*)-Ethylidene]bicyclo[3.3.0]octan-2-one (40)**: 35 mg (78%) from 56 mg (0.3 mmol) of the chloro ketone **33**; distillation temperature 40–50 °C (0.2 Torr); IR (neat) 1730, 1130 cm^{-1}; ^1H NMR (400 MHz) δ 1.68 (dt, 3 H, J = 7, 1.5 Hz), 1.75–1.95 (m, 3 H), 2.15–2.37 (m, 5 H), 2.64–2.71 (m, 1 H), 3.32–3.40 (m, 1 H), 5.36 (tq, 1 H, J = 1.5, 7 Hz); exact mass calcd for $C_{10}H_{14}O$ 150.1045, found 150.1044.

***cis*-6-[(*Z*)-Ethylidene]-5-methylbicyclo[3.3.0]octan-2-one (41)**: 42 mg (86%) from 60 mg (0.3 mmol) of the chloro ketone **34**; distillation temperature 40–50 °C (0.2 Torr); IR (neat) 1730, 1140 cm^{-1}; ^1H NMR (400 MHz) δ 1.30 (s, 3 H), 1.74 (dt, 3 H, J = 7, 2 Hz), 1.81–1.88 (m, 2 H), 1.92–2.01 (m, 1 H), 2.18–2.29 (m, 3 H), 2.34–2.43 (m, 3 H), 5.36 (br q, 1 H, J = 7 Hz); exact mass calcd for $C_{11}H_{16}O$ 164.1202, found 164.1202.

***cis*-6-[(*Z*)-Ethylidene]-1-methylbicyclo[3.3.0]octan-2-one (42)**: 39 mg (79%) from 60 mg (0.3 mmol) of the chloro ketone **35**; distillation temperature 45–60 °C (0.2 Torr); IR (neat) 1725, 1105 cm^{-1}; ^1H NMR (400 MHz) δ 1.11 (s, 3 H), 1.41–1.49 (m, 1 H), 1.66 (br d, 3 H, J = 7 Hz), 1.69–1.79 (m, 1 H), 1.87–1.94 (m, 1 H), 2.14–2.39 (m, 5 H), 2.88–2.94 (m, 1 H), 5.35 (br q, 1 H, J = 7 Hz); exact mass calcd for $C_{11}H_{16}O$ 164.1202, found 164.1200.

The Tricyclic Ketone 43: 48 mg (85%) from 68 mg (0.3 mmol) of the chloro ketone **36**; distillation temperature 65–80 °C (0.2 Torr); IR (neat) 1725, 1135 cm^{-1}; ^1H NMR (400 MHz) δ 1.39–1.47 (m, 1 H), 1.70–1.80 (m, 6 H), 1.89–2.00 (m, 2 H), 2.10–2.23 (m, 4 H), 2.28–2.35 (m, 2 H), 2.50 (dd, 1 H, J = 9, 18 Hz), 2.75–2.82 (m, 1 H), 5.37 (tq, 1 H, J = 2, 7 Hz); exact mass calcd for $C_{13}H_{18}O$ 190.1358, found 190.1358.

The Bicyclic Ketone 54: 645 mg (92%) from 825 mg (3.4 mmol) of the chloro ketone **53**; distillation temperature 70–80 °C (0.2 Torr); IR (neat) 1705, 1245 cm^{-1}; ^1H NMR (400 MHz) δ 0.86, 0.98 (d, d, 3 H each, J = 7 Hz in each case), 1.43–1.53 (m, 2 H), 1.63 (dt, 3 H, J = 7, 1.5 Hz), 1.84–2.01 (m, 4 H), 2.22–2.37 (m,

2 H), 2.49–2.58 (m, 2 H), 2.63 (br q, 1 H, J = 7 Hz), 2.88 (br dd, 1 H, J = 7, 10 Hz), 5.33 (tq, 1 H, J = 1.5, 7 Hz). Decoupling experiments: irradiation at δ 2.88 collapsed the br q at 2.63 to a br t (J = 7 Hz) and sharpened the multiplets at 2.49–2.58 and 1.43–1.53, while irradiation at δ 2.63 simplified the signal at 2.88 to a br d (J = 10 Hz) and sharpened the multiplets at 2.22–2.33 and 2.49–2.58. NOE difference experiment: irradiation at δ 2.88 caused signal enhancement at 2.63, 1.63, and 0.86; exact mass calcd for $C_{14}H_{22}O$ 206.1672, found 206.1666.

(1*S*,6*S*)-7-[(*Z*)-Ethylidene]-6-methylbicyclo[4.3.0]nonan-2-one (47). To a stirred solution of K_2CO_3 (264 mg, 1.6 mmol) in 4 mL of aqueous methanol (argon atmosphere) was added a solution of the enantiomerically pure acetate **44**[14] (89 mg, 0.4 mmol) in 2 mL in methanol and the solution was stirred at room temperature for 24 h. The mixture was diluted with water and extracted thoroughly with Et_2O. The combined extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. Distillation (80–90 °C (0.4 Torr)) of the residual oil gave 63 mg (88%) of the alcohol **45** as a colorless oil: ^1H NMR (400 MHz) δ 0.90 (s, 3 H), 1.09–1.78 (m, 10 H), 1.82–1.90 (m, 1 H), 1.99–2.08 (m, 1 H), 2.13–2.30 (m, 2 H), 2.38–2.48 (m, 1 H), 3.64 (dt, 1 H, J = 5.5, 11 Hz), 5.14 (tq, 1 H, J = 2, 7 Hz).

To a stirred solution–suspension of PCC (97 mg, 0.45 mmol) and NaOAc (7 mg, 0.09 mmol) in 2 mL of dry CH_2Cl_2 was added a solution of the alcohol **45** (54 mg, 0.3 mmol) in 0.5 mL of dry CH_2Cl_2 and the mixture was stirred at room temperature for 2 h. Dry Et_2O (10 mL) was added and the supernatant solution was decanted from a black gum. The latter material was stirred with 5 mL of dry Et_2O and the organic solution was again decanted. The combined organic solutions were passed through a short column of Florisil (3 g, elution with Et_2O). Concentration of the combined eluate, followed by distillation (50–65 °C (0.2 Torr)) of the remaining pale yellow oil, afforded 42 mg (79%) of the trans bicyclic ketone **46**: ^1H NMR (400 MHz) δ 0.88 (s, 3 H), 1.61–1.85 (m, 5 H), 1.89–2.15 (m, 3 H), 2.22–2.34 (m, 3 H), 2.37–2.48 (m, 2 H), 2.60 (dd, 1 H, J = 6, 12 Hz), 5.21 (tq, 1 H, J = 2, 7 Hz).

A mixture of 1% aqueous KOH (1 mL) and ethanol (15 mL) was stirred for 5 min. To 5 mL of this solution (argon atmosphere) was added a solution of the bicyclic ketone **46** (25 mg, 0.14 mmol) in 0.5 mL of ethanol, and the mixture was stirred at room temperature for 3.5 h. The solution was diluted with water and extracted thoroughly with Et_2O. The combined extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. Distillation (50–60 °C (0.2 Torr)) of the remaining oil gave 20 mg (79%) of the ketone **47** as a colorless oil. This substance exhibited IR and ^1H NMR spectra identical with those of the racemic annulation product **38**.

Preparation of the Ketal 55. A stirred solution of the bicyclic ketone **54** (1.0 g, 4.85 mmol), ethylene glycol (0.9 g, 14.5 mmol), and pyridinium *p*-toluenesulfonate (365 mg, 1.46 mmol) in 55 mL of benzene (argon atmosphere) was refluxed under a Dean–Stark water trap for 2.5 h. The solvent was removed and 60 mL of Et_2O was added to the residue. The resultant solution was washed (saturated $NaHCO_3$–H_2O, brine), dried ($MgSO_4$), and concentrated. Distillation (115–125 °C (0.3 Torr)) of the remaining oil provided 1.14 g (94%) of the ketal **55**, a colorless oil: IR (neat) 1440, 1145, 1105 cm^{-1}; ^1H NMR (400 MHz) δ 0.84, 0.90 (d, d, 3 H each, J = 7 Hz in each case), 1.11 (tt, 1 H, J = 3, 11 Hz), 1.33 (dq, 1 H, J = 4, 11 Hz), 1.55–1.85 (m, 9 H), 2.00–2.09 (m, 1 H), 2.14–2.23 (m, 1 H), 2.41–2.50 (m, 1 H), 2.61 (dd, 1 H, J = 7, 11 Hz), 3.94 (br s, 4 H), 5.24 (q, 1 H, J = 7 Hz). Decoupling experiments: irradiation at δ 2.61 simplified the signal at 2.00–2.09 to a br t (J = 8 Hz) and the signal at 1.11 to a td (J = 3, 11 Hz), while irradiation at δ 2.04 converted the dd at 2.61 to a d (J = 11 Hz) and sharpened the multiplet at 1.55–1.85; exact mass calcd for $C_{16}H_{26}O_2$ 250.1934, found 250.1938.

Hydroboration of the Ketal Alkene 55. Preparation of the Alcohols 56 and 57. To a cold (0 °C), stirred solution of the ketal alkene **55** (500 mg, 2.0 mmol) in 8 mL of dry THF (argon atmosphere) was added, dropwise, BH_3·Me_2S (300 μL, 3 mmol), and the solution was stirred at 0 °C for 30 min and at room temperature for 3.5 h. Sufficient water was added to destroy the excess reagent. Aqueous NaOH (3 M, 1.0 mL, 3 mmol) was added slowly, the solution was cooled to 0 °C, 30% aqueous H_2O_2 (1.0 mL, 8.8 mmol) was added dropwise, and the solution was heated at 40–50 °C for 1 H. Saturated NH_4Cl–H_2O (4 mL) and Et_2O (10 mL) were added and the phases were separated. The aqueous layer was extracted thoroughly with 1:1 Et_2O–petroleum ether. The combined extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. Flash chromatography (28 g of silica gel, 11:9 petroleum ether–Et_2O) of the residual material provided two products.

The less polar alcohol **56** (distillation temperature 148–158 °C (0.3 Torr), 444 mg, 83%), a colorless oil, exhibited IR (neat) 3450, 1380, 1120 cm^{-1}; ^1H NMR (400 MHz) δ 0.79, 0.94, 1.20 (d, d, d, 3 H each, J = 7 Hz in each case), 1.25–1.36 (m, 1 H), 1.49 (tt, 1 H, J = 3, 11 Hz), 1.59–1.85 (m, 8 H), 1.89–1.96 (m, 1 H), 2.13 (ddd, 1 H, J = 7, 8, 11 Hz), 2.24–2.31 (m, 1 H), 2.99 (br s, 1 H, exchanges with D_2O); 3.90–3.99 (m, 4 H), 3.99–4.05 (m, 1 H). Decoupling experiments: irradiation at δ 4.02 simplified the multiplet at 1.89–1.96 to a q (J = 8 Hz) and the doublet at 1.20 to a s, irradiation at δ 1.92 sharpened the signal at 2.24–2.31 and simplified the signals at 3.99–4.05 and 2.13 to a q (J = 7 Hz) and a dd (J = 7, 11 Hz), respectively, and irradiation at δ 2.13 sharpened the multiplet at 1.89–1.96 and changed the tt at 1.49 to a td (J = 3, 11 Hz); exact mass calcd for $C_{13}H_{28}O_3$ 268.2039, found 268.2033.

The more polar alcohol **57** (distillation temperature 150–160 °C (0.3 Torr), 20 mg, 4%), a colorless oil, exhibited IR (neat) 3450, 1370, 1100 cm^{-1}; ^1H NMR (400 MHz) δ 0.89, 0.94, 1.18 (d, d, d, 3 H each, J = 7 Hz in each case), 1.05 (tt, 1 H, J = 3, 11 Hz), 1.26–1.38 (m, 2 H), 1.52–1.64 (m, 5 H), 1.77–1.89 (m, 5 H), 1.99 (dd, 1 H, J = 6, 11 Hz), 3.64–3.71 (m, 1 H), 3.88–4.00 (m, 4 H); exact mass calcd for $C_{16}H_{28}O_3$ 268.2039, found 268.2043.

Preparation of the Keto Alcohols 58 and 59. A stirred solution of the ketal alcohol **56** (402 mg, 1.5 mmol) water (1.5 mL), and pyridinium *p*-toluenesulfonate (113 mg, 0.45 mmol) in 13.5 mL of acetone (argon atmosphere) was refluxed for 2 h. The solvent was removed under reduced pressure and 45 mL of Et_2O was added to the residue. The resultant solution was washed (aqueous $NaHCO_3$, brine), dried ($MgSO_4$), and concentrated. Analysis (GLC) of the remaining yellow oil (311 mg, 92%) showed that it consisted of a 1:2[33] mixture of **58** and **59**, respectively. This material was dissolved in 3 mL of dry MeOH and a solution of NaOMe (0.42 mmol) in 2 mL of dry MeOH was added. The mixture was stirred (argon atmosphere) at room temperature for 3.5 h. Saturated NH_4Cl–H_2O (2 mL) and Et_2O (10 mL) were added and the aqueous phase was extracted thoroughly with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Distillation (140–150 °C (0.3 Torr)) of the oil thus obtained afforded 270 mg (80%) of a 1:3 mixture of the keto alcohols **58** and **59**: IR (neat) 3450, 1700, 1370, 1110 cm^{-1}; ^1H NMR (400 MHz) δ 0.79, 0.92 (d, d, ratio 3:1, 3 H, J = 7 Hz), 1.00, 1.02 (d, d, ratio 1:3, 3 H, J = 7 Hz), 1.15, 1.17 (d, d, ratio 1:3, 3 H, J = 7 Hz), 1.05–2.55 (m, 13 H), 2.69–2.76, 2.99–3.07 (m, m, ratio 1:3, 1 H), 3.90–3.97, 4.19–4.27 (m, m, ratio 1:3, 1 H); exact mass calcd for $C_{14}H_{24}O_2$ 224.1777, found 224.1774.

Preparation of the Alkene Alcohols 60 and 61. To a stirred solution of $NaCH_2SOCH_3$ (3 mmol) in 12 mL of dry dimethyl sulfoxide (DMSO) (argon atmosphere) was added a solution of $[Ph_3PMe]Br$ (1.11 g, 3.1 mmol) in 5 mL of dry DMSO; the mixture was stirred at room temperature for 10 min. A solution of a 1:3 mixture of the keto alcohols **58** and **59** (224 mg, 1 mmol) in 5 mL of dry DMSO was added and stirring was continued for 16 h. The solution was poured into ice–water and the resultant mixture was extracted thoroughly with pentane. The combined extracts were washed (1:1 DMSO–water, water, brine), dried ($MgSO_4$), and concentrated. Flash chromatography (18 g of silica gel, 4:1 petroleum ether–Et_2O) of the remaining yellow oil gave two products.

The less polar alkene alcohol **61** (distillation temperature 75–90 °C (0.1 Torr), 168 mg, 76%) exhibited IR (neat) 3350, 1635, 890 cm^{-1}; ^1H NMR (400 MHz) δ 0.76, 0.97, 1.14 (d, d, d, 3 H each, J = 7 Hz in each case), 1.00 (d, 1 H, J = 6 Hz, exchanges with D_2O), 1.05 (dq, 1 H, J = 4, 11 Hz), 1.20 (dt, 1 H, J = 8, 11 Hz), 1.49 (br t, 1 H, J = 8 Hz), 1.65–2.03 (m, 8 H), 2.30–2.39 (m, 2 H), 4.15–4.22 (m, 1 H), 4.51, 4.61 (d, d, 1 H each, J = 2 Hz in each case). Decoupling experiments: irradiation at δ 2.34 simplified the signals at 1.05 and 1.20 to a q (J = 11 Hz) and a dd (J = 8, 11 Hz), respectively, and sharpened the multiplet at 1.65–2.03, while irradiation at δ 4.19 collapsed the resonances at 1.10 and

(33) This ratio varied slightly from experiment to experiment.

1.14 to singlets and sharpened the multiplet at 1.65–2.03; exact mass calcd for $C_{15}H_{26}O$ 222.1985, found 222.1981.

The more polar alkene alcohol **60** (distillation temperature 80–90 °C (0.1 Torr), 10 mg, 4%) exhibited IR (neat) 3350, 1635, 880 cm^{-1}; ^1H NMR (400 MHz) δ 0.79, 0.93, 1.20 (d, d, d, 3 H each, J = 7 Hz in each case), 1.12–1.19 (m, 1 H), 1.31–1.39 (m, 2 H), 1.63–1.85 (m, 6 H), 1.92–1.99 (m, 1 H), 2.06 (ddd, 1 H, J = 7, 8, 10 Hz), 2.14–2.33 (m, 2 H), 2.65–2.71 (m, 1 H), 3.92–4.00 (m, 1 H), 4.69 (br s, 1 H), 4.71 (br s, 1 H). Decoupling experiments: irradiation at δ 3.96 simplified the signals at 1.92–1.99 and 1.20 to a q (J = 8 Hz) and a s, respectively, while irradiation at δ 2.68 changed the resonance at 2.06 to a dd (J = 7, 10 Hz) and sharpened the multiplet at 1.63–1.85; exact mass calcd for $C_{15}H_{26}O$ 222.1985, found 222.1983.

(±)-3-*epi*-Anhydrooplopanone (62). Oxidation of the alkene alcohol **61** with PCC was accomplished via a procedure very similar to that described earlier (preparation of **46**). From 120 mg (0.54 mmol) of **61** there was obtained 111 mg (93%) of **62** as a colorless oil, distillation temperature 100–115 °C (0.3 Torr): IR (neat) 3060, 1710, 1645, 885 cm^{-1}; ^1H NMR (400 MHz) δ 0.76, 0.90 (d, d, 3 H each, J = 7 Hz in each case), 0.98 (dq, 1 H, J = 4, 12 Hz), 1.27 (dt, 1 H, J = 7, 12 Hz), 1.54–1.77 (m, 4 H), 1.81 (tt, 1 H, J = 3, 12 Hz), 1.87–1.94 (m, 1 H), 1.98–2.07 (m, 2 H), 2.17 (s, 3 H), 2.33 (td, 1 H, J = 4, 13 Hz), 2.46–2.57 (m, 1 H), 3.15 (ddd, 1 H, J = 4, 7, 9 Hz), 4.53, 4.63 (d, d, 1 H each, J = 2 Hz in each case). Decoupling experiments: irradiation at δ 3.15 changed the dt at 1.27 to a t (J = 12 Hz) and sharpened the signal at 1.98–2.07, irradiation at δ 2.52 changed the resonances at 1.87–1.94 and 1.27 to a t (J = 9 Hz) and a dd (J = 7, 12 Hz), respectively, irradiation at δ 1.27 simplified the signals at 3.15, 2.46–2.57, and 1.81 to a dd (J = 4, 9 Hz), a br t (J = 9 Hz), and a td (J = 3, 12 Hz), respectively, and irradiation at δ 0.98 changed the signals at 2.33 and 1.81 to a dd (J = 4, 13 Hz) and a td (J = 3, 12 Hz), respectively. NOE difference experiment: irradiation at δ 1.27 enhanced the signals at 3.15, 0.98, and 0.76; exact mass calcd for $C_{15}H_{24}O$ 220.1828, found 220.1826.

(±)-Anhydrooplopanone (51). A stirred solution of the ketone **62** (98 mg, 0.45 mmol) and NaOMe (0.17 mmol) in 4 mL of dry MeOH (argon atmosphere) was heated to 60 °C for 24 h. The solution was cooled to room temperature and 2 mL of saturated NH_4Cl-H_2O and 10 mL of Et_2O were added. The aqueous phase was extracted with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Analysis (GLC) of the remaining oil indicated that it consisted of a 93:7 mixture of (±)-anhydrooplopanone (**51**) and the starting material **62**. Recrystallization of this material from petroleum ether provided 81 mg (82%) of (±)-**51**, mp 68 °C: IR ($CHCl_3$) 3060, 1705, 1645, 885 cm^{-1}; ^1H NMR (400 MHz) δ 0.66, 0.91 (d, d, 3 H each, J = 7 Hz in each case), 1.11 (dq, 1 H, J = 4, 11 Hz), 1.27 (tt, 1 H, J = 3, 11 Hz), 1.50–1.76 (m, 5 H), 1.81 (ddd, 1 H, J = 5, 7, 11 Hz), 1.87–2.04 (m, 3 H), 2.18 (s, 3 H), 2.37 (ddd, 1 H, J = 3, 4, 13 Hz), 2.71 (dt, 1 H, J = 5, 11 Hz), 4.57, 4.67 (d, d, 1 H each, J = 2 Hz in each case). Decoupling experiments: irradiation at δ 2.71 sharpened the multiplets at 1.50–1.76 and 1.87–2.04, irradiation at δ 2.37 simplified the dq at 1.11 to a q (J = 11 Hz) and sharpened the multiplet at 1.87–2.04, and irradiation at 1.27 changed the dq at 1.11 to a dt (J = 4, 11 Hz) and sharpened the multiplet at 1.50–1.76. ^{13}C NMR (75.6 MHz) δ 15.7 (q), 22.0 (q), 26.6 (t), 27.4 (t), 28.5 (t), 28.9 (q), 29.6 (d), 35.3 (t), 49.3 (d), 51.8 (d), 52.1 (d), 56.1 (d), 103.6 (t), 150.9 (s), 211.7 (s); exact mass calcd for $C_{15}H_{24}O$ 220.1828, found 220.1828. The ^1H NMR spectrum of (±)-**51** was identical with that of (−)-anhydrooplopanone.[26] The IR and ^{13}C NMR data derived from our synthetic material agreed well with those reported for (−)-anhydrooplopanone.[22]

Preparation of the Epoxy Alcohols 63 and 64. To a solution of the alkene alcohol **61** (53 mg, 0.24 mmol) in 3 mL of DMSO and 1 mL of water (argon atmosphere) was added, in one portion, *N*-bromosuccinimide (86 mg, 0.48 mmol); the mixture was stirred at room temperature for 45 min. Saturated $NaHCO_3$-H_2O (2 mL) and water (2 mL) were added and the mixture was extracted thoroughly with Et_2O. The combined organic extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. The remaining pale yellow oil was dissolved in 3 mL of MeOH containing 67 mg (0.48 mmol) of K_2CO_3, and the mixture was stirred vigorously for 1.5 h. The reaction mixture was diluted with water and extracted with Et_2O. The combined organic extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. Flash chromatography (12 g of silica gel, 7:3 petroleum ether–Et_2O) of the resultant pale yellow oil afforded two products.

The minor, less polar epoxy alcohol **64** (7 mg, 12%) was recrystallized from petroleum ether and exhibited mp 92.5–93 °C: IR ($CHCl_3$) 3590, 3350, 3000, 1240, 900 cm^{-1}; ^1H NMR (300 MHz) δ 0.81, 0.97, 1.14 (d, d, d, 3 H each, J = 7 Hz in each case), 1.10–1.72 (m, 10 H), 1.80–2.05 (m, 3 H), 2.30 (dt, 1 H, J = 8, 11 Hz), 2.57, 2.66 (d, d, 1 H each, J = 5 Hz in each case), 4.16 (br q, 1 H, J = 7 Hz); exact mass calcd for $C_{15}H_{26}O_2$ 238.1934, found 238.1935.

The major, more polar epoxy alcohol **63** (36 mg, 63%) was recrystallized from petroleum ether and exhibited mp 91 °C: IR ($CHCl_3$) 3590, 3450, 3040, 840 cm^{-1}; ^1H NMR (300 MHz) δ 0.79, 0.98, 1.14 (d, d, d, 3 H each, J = 7 Hz in each case), 1.18–1.45 (m, 4 H), 1.58–2.05 (m, 9 H), 2.34 (dt, 1 H, J = 7, 11 Hz), 2.48 (d, 1 H, J = 5 Hz), 2.86 (dd, 1 H, J = 2, 5 Hz), 4.16 (br q, 1 H, J = 7 Hz); exact mass calcd for $C_{15}H_{26}O_2$ 238.1934, found 238.1933.

Preparation of the Diol 65. To a cold (0 °C), stirred solution of $LiAlH_4$ (6 mg, 0.15 mmol) in 2 mL of dry Et_2O (argon atmosphere) was added a solution of the epoxy alcohol **63** (33 mg, 0.14 mmol) in 2 mL of dry Et_2O. The mixture was stirred at room temperature for 1 h. Workup as described previously (preparation of **17**), followed by recrystallization of the resultant white solid from petroleum ether–Et_2O, gave 32 mg (96%) of the diol **65** as needles, mp 117–118 °C: IR ($CHCl_3$) 3590, 3400, 1370, 1120, 890 cm^{-1}; ^1H NMR (400 MHz) δ 0.78, 0.94, 1.12 (d, d, d, 3 H each, J = 7 Hz in each case), 1.07 (dq, 1 H, J = 4, 11 Hz), 1.08 (s, 3 H), 1.24–1.41 (m, 4 H), 1.51 (tt, 1 H, J = 3, 11 Hz), 1.60–2.00 (m, 8 H), 4.11 (dq, 1 H, J = 1, 7 Hz); exact mass calcd for $C_{14}H_{25}O_2$ (M^+ − Me) 225.1856, found 225.1852.

(±)-3-*epi*-Oplopanone (66). Oxidation of the diol **65** with PCC was accomplished via a procedure very similar to that described previously (preparation of **46**). From 28 mg (0.12 mmol) of the diol **65** there was obtained, after distillation (85–95 °C (0.2 Torr)) of the crude product, 26 mg (94%) of the keto alcohol **66** as a white solid that exhibited mp 68 °C: IR ($CHCl_3$) 3590, 3450, 1700, 1385, 1370, 1360 cm^{-1}; ^1H NMR (400 MHz) δ 0.79, 0.89 (d, d, 3 H each, J = 7 Hz in each case), 1.01 (dq, 1 H, J = 4, 11 Hz), 1.09 (s, 3 H), 1.33–1.49 (m, 4 H), 1.57–1.73 (m, 4 H), 1.77 (td, 1 H, J = 3, 13 Hz), 1.83–2.00 (m, 2 H), 2.08 (dt, 1 H, J = 7, 11 Hz), 2.16 (s, 3 H), 3.13 (ddd, 1 H, J = 4, 7, 9 Hz); exact mass calcd for $C_{15}H_{26}O_2$ 238.1934, found 238.1945.

(±)-Oplopanone (50). A solution of (±)-3-*epi*-oplopanone (**66**) (10 mg, 0.04 mmol) and NaOMe (0.04 mmol) in 2.5 mL of dry MeOH (argon atmosphere) was stirred at 40–45 °C for 36 h. Workup as described previously (preparation of **51**) gave a solid that, on the basis of analysis by GLC, consisted of a 94:6 mixture of (±)-oplopanone (**50**) and the starting material **66**. Recrystallization of this material from hexane-Et_2O gave 9 mg (90%) of (±)-**50** as colorless needles, mp 99–100 °C: IR ($CHCl_3$) 3590, 3450, 1710, 1465, 1385, 1370, 1360 cm^{-1}; ^1H NMR (400 MHz) δ 0.70, 0.90 (d, d, 3 H each, J = 7 Hz in each case), 1.04–1.17 (m, 2 H), 1.20 (s, 3 H), 1.35–1.63 (m, 7 H), 1.77–1.87 (m, 3 H), 1.96 (br q, 1 H, J = 11 Hz), 2.19 (s, 3 H), 2.66 (ddd, 1 H, J = 6, 9, 11 Hz); ^{13}C NMR (75.6 MHz) δ 15.6 (q), 20.3 (q), 22.0 (q), 23.0 (t), 25.3 (t), 28.6 (t), 29.6 (q), 29.7 (d), 42.1 (t), 46.7 (d), 49.5 (d), 55.8 (d), 57.0 (d), 73.1 (s), 211.5 (s); exact mass calcd for $C_{15}H_{26}O_2$ 238.1934, found 238.1932. Our synthetic (±)-**50** exhibited spectra identical with those of (−)-oplopanone[29] and a previously synthesized sample of (±)-oplopanone.[29] Also, the melting point of our synthetic material agreed well with those reported (101.5–102 °C,[19] 97–98 °C[20]) previously for (±)-**50**.

Preparation of the Epoxy Alcohol 64. To a cold (ice–salt bath), stirred solution of dimethylsulfonium methylide[31] (1.2 mmol) in a mixture of dry DMSO (5 mL) and dry THF (4 mL) (argon atmosphere) was added a solution of 90 mg (0.4 mmol) of a 1:3 mixture of the keto alcohols **58** and **59** in 3 mL of dry DMSO. The mixture was stirred for 30 min, warmed to room temperature, and then sitrred for a further 8 h. Saturated NH_4Cl-H_2O (3 mL) and pentane (15 mL) were added and the aqueous phase was extracted thoroughly with Et_2O. The combined organic extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. Flash chromatography (10 g of silica gel, 2:1 petroleum ether–Et_2O) of the residual oil, followed by recrystallization (petroleum ether) of the solid thus obtained, provided 66 mg (69%) of the epoxy alcohol **64** as colorless needles, mp 92.5–93

°C. This material exhibited spectral data identical with those of the minor epoxide **64** obtained from the olefinic alcohol **61** (vide supra).

Preparation of the Diol 71. Reduction of the epoxy alcohol **64** with $LiAlH_4$ was achieved via a procedure identical with that described previously (preparation of **65**). From 34 mg (0.14 mmol) of **64** there was obtained 31 mg (91%) of the diol **71** as a glassy, low-melting solid, distillation temperature 100–110 °C (0.3 Torr): IR ($CHCl_3$) 3600, 3450, 1370, 880 cm^{-1}; ^1H NMR (300 MHz) δ 0.81, 0.93, 1.13 (d, d, d, 3 H each, J = 7 Hz in each case), 1.18 (s, 3 H), 1.20–2.05 (m, 15 H), 4.11 (br q, 1 H, J = 7 Hz); exact mass calcd for $C_{14}H_{25}O_2$ (M^+ – Me) 225.1856, found 225.1859.

(±)-3,8-Di-*epi*-oplopanone (72). Oxidation of the diol **71** with PCC was accomplished via a procedure very similar to that described previously (preparation of **46**). From 29 mg (0.12 mmol) of the diol **71** there was obtained 27 mg (91%) of the keto alcohol **72** as a colorless oil, distillation temperature 100–110 °C (0.3 Torr): IR (neat) 3450, 1700, 1360 cm^{-1}; ^1H NMR (300 MHz) δ 0.82, 0.89 (d, d, 3 H each, J = 7 Hz in each case), 1.08 (br s, 1 H, exchanges with D_2O), 1.20 (s, 3 H), 1.16–2.00 (m, 12 H), 2.16 (s, 3 H), 3.14 (ddd, 1 H, J = 4, 7, 9 Hz); exact mass calcd for $C_{15}H_{26}O_2$ 238.1934, found 238.1932.

(±)-8-*epi*-Oplopanone (70). A solution of (±)-3,8-di-*epi*-oplopanone (**72**) (23 mg, 0.10 mmol) and NaOMe (0.04 mmol) in 2.5 mL of dry MeOH (argon atmosphere) was stirred at 60 °C for 24 h. Workup as described previously (preparation of **51**) gave a yellow oil that, on the basis of analysis by GLC, consisted of a 93:7 mixture of (±)-8-*epi*-oplopanone (**70**) and the starting material **72**. Flash chromatography (6 g of silica gel, 11:9 petroleum ether–Et_2O), followed by recrystallization (hexane–Et_2O) of the solid thus obtained, gave 19 mg (84%) of (±)-**70**, mp 62 °C: IR ($CHCl_3$) 3590, 3450, 1705, 1465, 1390, 1375, 1360 cm^{-1}; ^1H NMR (400 MHz) δ 0.72, 0.90 (d, d, 3 H each, J = 7 Hz in each case, 1.07 (tt, 1 H, J = 3, 11 Hz), 1.22 (s, 3 H), 1.29–1.37 (m, 4 H), 1.43–1.63 (m, 4 H), 1.70–1.77 (m, 2 H), 1.94 (ddd, 1 H, J = 4, 8, 11 Hz), 2.02 (q, 1 H, J = 11 Hz), 2.19 (s, 3 H), 2.60 (dt, 1 H, J = 5, 11 Hz). Decoupling experiments: irradiation at δ 2.60 changed the q at 2.02 to a t (J = 11 Hz) and sharpened the signal at 1.43–1.63, while irradiation at δ 1.07 also changed the q at 2.02 to a t (J = 11 Hz) and sharpened the multiplets at 1.29–1.37, 1.43–1.63, and 1.70–1.77. ^{13}C NMR (75.6 MHz) δ 15.8 (q), 20.7 (t), 21.9 (q), 24.5 (t), 28.2 (q), 28.7 (t), 29.0 (q), 29.7 (d), 40.0 (t), 44.8 (d), 49.4 (d), 55.7 (d), 56.1 (d), 70.4 (s), 212.1 (s); exact mass calcd for $C_{15}H_{26}O_2$ 238.1934, found 238.1929.

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Supplementary Material Available: ^1H NMR spectra of compounds **8**, **10**, **14–17**, **20**, **30–43**, **47**, **50**, **51**, **53–57**, **58** + **59** (mixture), **60–66**, and **70–72** (62 pages). Ordering information is given on any current masthead page.