A Novel Route to the Marasmane Skeleton via a Tandem Rearrangement−Cyclopropanation Reaction. Total Synthesis of (+)-Isovelleral

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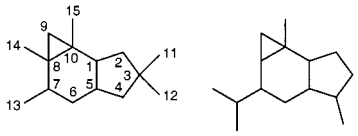
A general and efficient route to the marasmane skeleton is described. Total syntheses of two simple marasmanes (**35** and **37**) in racemic form were achieved using a MgI_2-catalyzed rearrangement−cyclopropanation reaction of trimethylsilyl enol ether **31** derived from naphthalenone **30**. The reaction proceeds in high yield with complete diastereoselectivity and does not require the use of special cyclopropanation reagents. Application of this novel route to the marasmane framework was extended to the synthesis of naturally occurring (+)-isovelleral (**41**).

Introduction

The majority of marasmane sesquiterpenes found in nature have been isolated from basidiomycete species belonging to the genus *Lactarius*.[1] Since a considerable number of these secondary metabolites exhibit antifeedant, antifungal, and antibacterial activities, these sesquiterpenes may take part in the chemical defense system of the basidiomycete against predators.[2] Despite their interesting physiological activities and unusual tricyclic cyclopropa[*e*]indene framework, relatively few total syntheses of natural marasmanes have been published.[1b]



marasmane ivaxillarane

The tricyclic core of marasmanes[3] is also present in sesquiterpenes belonging to the very small group of ivaxillaranes.[4] Although not aiming at synthesizing an ivaxillarane sesquiterpene, Howard and Fenical[5] found that solvolytic rearrangement of the naturally occurring brominated eudesmane **1** resulted in a ca. 70% yield of a 3:2 mixture of guaiane **4** and the ivaxillarane derivative **5**, respectively, the latter with unknown orientation of the cyclopropane ring (Scheme 1). The outcome of this reaction suggests that it might be possible to convert an appropriately functionalized bicyclic octahydronaphthalene system to the tricyclic cyclopropa[*e*]indene system present in marasmanes in a single step. Herein, we report a novel synthetic approach to marasmanes using a tandem rearrangement−cyclopropanation sequence as key step.

Mesylate **6** possessing an allylic OH group at C6 is a suitable substrate for studying this novel route to the marasmane skeleton (Scheme 2). The C-6α orientation of the OH group in **6** is essential because a β OH group at that position would probably result in the formation of a bridged ether.[6] Previous studies on the chemical consequences of through-bond interactions (TBI) in trans-fused perhydronaphthalene-1,4-diol monosulfonate esters[7] suggested that deprotonation of the OH group in **6** in refluxing benzene or toluene would induce ionization of the sulfonate ester bond and rearrangement to the homoallylic cation **7**. Successive rearrangement of **7** to cyclopropylcarbinyl cation **8**[8] followed by a stabilizing C6 → C7 1,2-H shift[9] would give the marasmane ketone **9**. Because exploratory ab initio calculations indicated that the cyclopropylcarbinyl cation **8** is more stable than the stereoisomeric cation with opposite orientation of the cyclopropane ring ($\Delta E = 31.3$ kcal mol^{-1}),[10] it was further

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(1) Vidari, G.; Vita-Finzi, P. *Studies in Natural Product Chemistry*; Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1995; Vol. 17, pp 153−206. (b) Daniewski, W. M.; Vidari, G. *Progr. Chem. Org. Nat. Prod.* **1999**, *77*, 69.

(2) Camazine, S. M.; Resch, J. F.; Eisner, T.; Meinwald, J. *J. Chem. Ecol.* **1983**, *9*, 1439. (b) Sterner, O.; Bergman, R.; Kihlberg, J.; Wickberg, B. *J. Nat. Prod.* **1985**, *48*, 279. (c) Sterner, O.; Bergman, R.; Franzen, C.; Wickberg, B. *Tetrahedron Lett.* **1985**, *26*, 3163. (d) Anke, H.; Sterner, O. *Planta Medica* **1991**, *57*, 344. (e) Daniewski, W. M.; Gumulka, M.; Pankowska, E.; Ptaszynska, K.; Bloszyk, E.; Jacobsson, U.; Norin, T. *Phytochemistry* **1993**, *32*, 1499. (f) Daniewski, W. M.; Gumulka, M.; Przesmycka, D.; Ptaszynska, K.; Bloszyk, E.; Drozdz, B. *Phytochemistry* **1995**, *38*, 1161.

(3) The numbering system used for the marasmane skeleton is based on the system adopted for naphthalene (see structure **6**) and will be followed throughout the text of this paper.

(4) Connolly, J. D.; Hill, R. A. *Dictionary of Terpenoids*; Chapman & Hall: London, 1991; Vol. I, pp 553−554.

(5) Howard, B. M.; Fenical, W. *J. Org. Chem.* **1977**, *42*, 2518.

(6) See Scheme 1 and ref 7e.

(7) Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; Brunekreef, G. A.; de Groot, A. *J. Org. Chem.* **1990**, *55*, 941. (b) Jenniskens, L. H. D.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1991**, *56*, 6585. (c) Orru, R. V. A.; Wijnberg, J. B. P. A.; Bouwman, C. T.; de Groot, A. *J. Org. Chem.* **1994**, *59*, 374. (d) Piet, D. P.; Orru, R. V. A.; Jenniskens, L. H. D.; van de Haar, C.; van Beek, T. A.; Franssen, M. C. R.; Wijnberg, J. B. P. A.; de Groot, A. *Chem. Pharm. Bull.* **1996**, *44*, 1400. (e) Bell, R. P. L.; Sobolev, A.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1998**, *63*, 122.

(8) Nagasawa, T.; Handa, Y.; Onoguchi, Y.; Suzuki, K. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 31.

(9) Tobe, Y.; Sato, J.-i.; Sorori, T.; Kakiuchi, K.; Odaira, Y. *Tetrahedron Lett.* **1986**, *27*, 2905.

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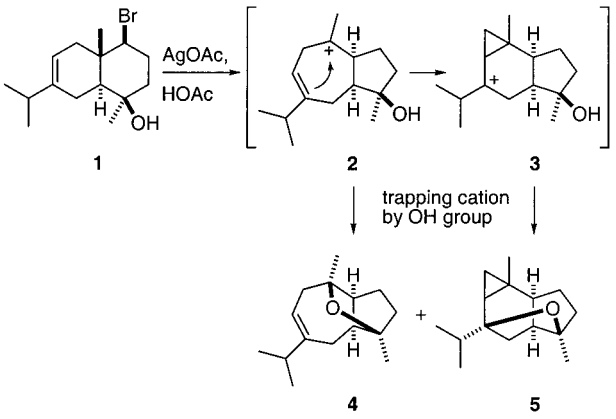
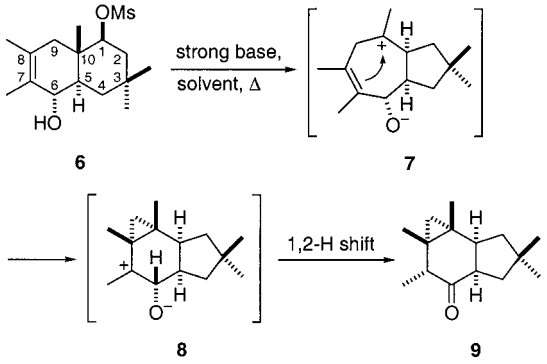
Scheme 1



1 2 3 4 5

Scheme 2



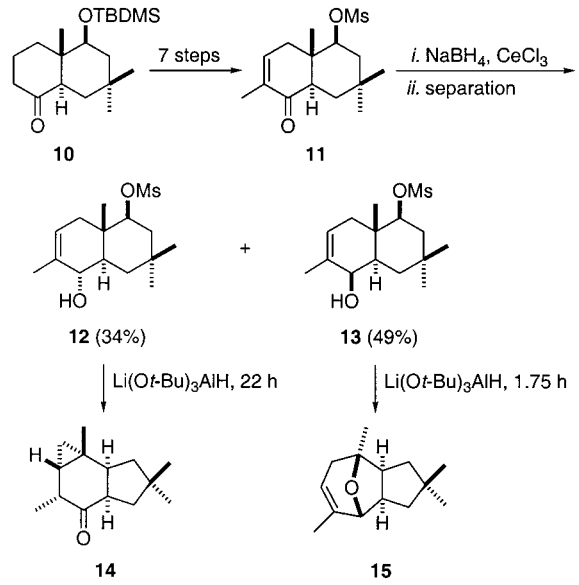
6 7 8 9

expected that **9** would have the same stereochemistry as found in naturally occurring marasmanes.

Results and Discussion

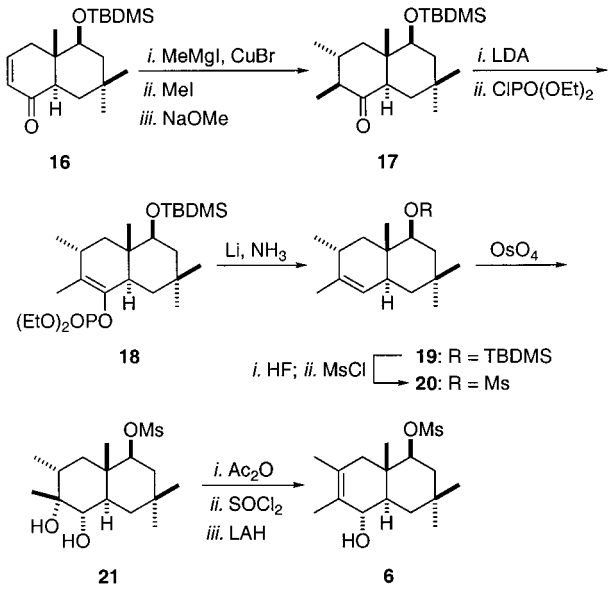
To establish reaction conditions that would allow selective formation of the tricyclic cyclopropa[*e*]indene core, a model study was carried out with mesylate **12**. The synthesis of **12**, structurally identical to **6** but lacking the Me group at C8, started with the known ketone **10**[7e] (Scheme 3). Following standard procedures, **10** was converted to enone **11** in 65% overall yield.[11] Reduction of **11** with $NaBH_4$ in the presence of $CeCl_3$[12] produced a separable mixture of **12** and its C6 epimer **13** in yields of 34 and 49%, respectively.[13] Improvement in the yield of **12** via Mitsunobu inversion[14] of **13** was unsuccessful. With the limited amount of **12** obtained from the reduction of **11**, we were able to demonstrate that the rearrangement−cyclopropanation reaction could be achieved by treating **12** with 2.5 equiv of Li(O*t*-Bu)$_3$AlH[15] in refluxing benzene for 22 h. Although a complex mixture was obtained, the tricyclic ketone **14** was isolated in acceptable yield (36%). The formation of ketone **14** can be explained by a mechanism analogous to that outlined in Scheme 2. Reduction of **14** by the bulky Li(O*t*-Bu)$_3$AlH did not occur because of steric hindrance. The identity of **14** was unambiguously established using NMR. The C−H coupling of ca. 160 Hz observed for both the C8 (d) and C9 (t) signals at δ 27.21 and 15.24, respectively, in the ^{1}H-coupled ^{13}C NMR spectrum is diagnostic for the presence of the trisubstituted cyclopropane ring in **14**. Additional support was obtained from the HETCOR spectrum in which C8 and C9 were correlated with the upfield-shifted signals at δ_H 1.00 and 0.33 and 0.08, respectively. A NOESY experiment, in which the expected key NOE correlations were observed, also confirmed the stereochemistry assigned to **14**. As predicted by ab initio calculations, this stereochemistry is the same as in naturally occurring marasmanes. The reaction of **13** with Li(O*t*-Bu)$_3$AlH yielded **15** in 68% as expected.

Scheme 3



10 11 14 15

Scheme 4



16 17 18 19 20 21 6

We next investigated the rearrangement−cyclopropanation reaction of mesylate **6**. In light of the rather poor yield of **12** via reduction of a carbonyl group (vide supra), introduction of the C-6α OH group in **6** was planned via osmylation (Scheme 4). A copper-catalyzed conjugate addition of MeMgI to the known enone **16**,[7e] trapping of

(10) The energy difference calculations were carried out with B3LYP/6-31G(d,p) using the GAUSSIAN 98 program (Revision A.7), Gaussian, Inc., Pittsburgh, PA, 1998.

(11) The experimental details are available as Supporting Information.

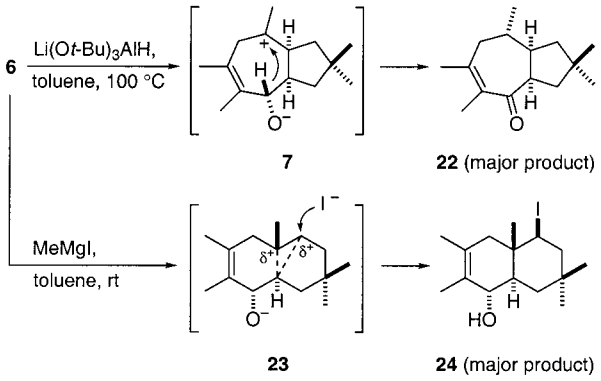
(12) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.

(13) Other reducing agents were also tried, but their use did not lead to improvement of the yield of **12**.

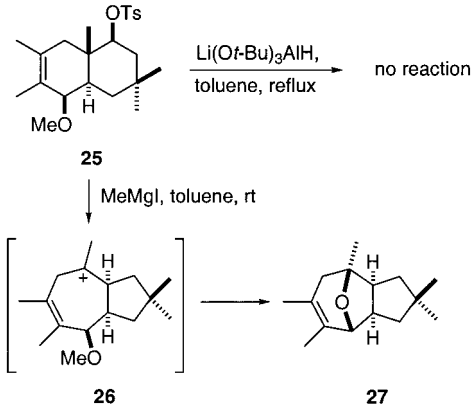
(14) Mitsunobu, O. *Synthesis* **1981**, 1.

(15) Li(O*t*-Bu)$_3$AlH was also employed successfully in the key step of the total synthesis of furanether B. See ref 7e.

Scheme 5



Scheme 6



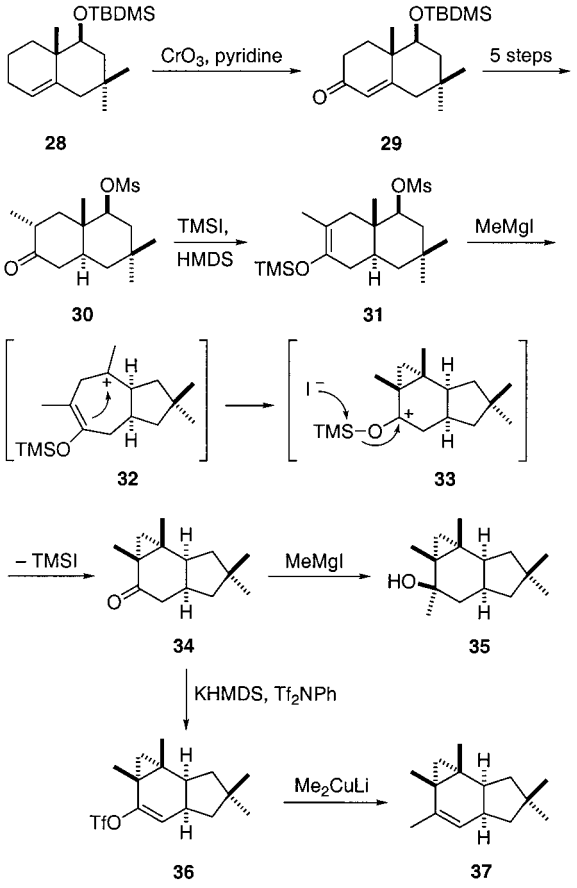
the resulting enolate by MeI, and subsequent epimerization afforded dimethylated ketone **17** in excellent yield. Treatment of **17** with LDA and trapping of the resulting enolate with diethyl chlorophosphate gave phosphate enol ester **18**[16] that was reduced with Li in NH_3[17] to afford olefin **19** as the sole product in 51% overall yield. Following standard procedures, **19** was further converted to mesylate **20**.[11] Using a stoichiometric amount of OsO_4,[18] dihydroxylation of **20** resulted in a 75% yield of diol **21**. The H-6 signal at δ 3.10 with a coupling of 10.7 Hz in the ^{1}H NMR spectrum of **21** confirmed the α orientation of the secondary OH group. Completion of the synthesis of **6** was accomplished in high yield by selective protection of the secondary OH group as its acetate, elimination of the tertiary OH group with $SOCl_2$, and reductive removal of the protecting acetyl group.

On exposure of **6** to Li(O*t*-Bu)$_3$AlH in toluene at 100 °C, a complex mixture was obtained with lactarane enone **22** (ca. 55%) as the major component and the desired ketone **9** in only trace amounts (Scheme 5). Apparently, a direct transannular C6 → C10 H shift (**7** → **22**) is energetically more favorable than cyclopropane ring formation (**7** → **8**, see Scheme 2). When MeMgI[19] was used instead of Li(O*t*-Bu)$_3$AlH, **6** reacted readily at room temperature, but the outcome was again disappointing. Although a small amount (6%) of ketone **9**[20] could be isolated, the major product (56%) was iodide **24**. The H-1 signal at δ 4.37 with a coupling of 13.0 Hz in the ^{1}H NMR spectrum indicates that formation of **24** had proceeded with retention of configuration suggesting involvement of the bridged-ion intermediate **23**. Iodide formation was also observed on reaction of alcohol **12** with MeMgI, but to a lesser extent (31%) than in the reaction of **6** (56%). On the other hand, the yield of rearrangement−cyclopropanation product in this reaction of **12** was higher (22% of **14** versus 6% of **9**). These findings suggest that steric repulsion between the Me groups at C8 and C10 in the transition state leading to intermediate **8** makes the reaction pathway to **9** energetically less favorable than the one to **14**. Chelation of the sulfonate ester with MeMgI or MgI_2[21] also present in the reaction medium via the Schlenk equilibrium may explain the ease by which **6** and **12** reacted with MeMgI at room temperature. Support for this view came from two experiments with tosylate **25** possessing a β MeO group at C6 through which TBI-induced ionization of the sulfonate ester bond can be ruled out.[22] On exposure to MeMgI at room temperature, **25** showed a fast rearrangement to bridged ether **27** (Scheme 6). On the other hand, as expected, no reaction took place when **25** was treated with Li(O*t*-Bu)$_3$AlH in refluxing toluene. These experiments on **25** clearly demonstrate that MeMgI is capable of inducing ionization of the sulfonate ester bond without involvement of TBI. Another important conclusion from the reaction of **25** with MeMgI is that rearrangement can compete favorably with iodide formation when the positive charge of the homoallylic cation is effectively stabilized. In case of **25** such an intramolecular stabilization occurs via trapping of cation **26** by the proximate MeO group (see Scheme 6). For a successful rearrangement−cyclopropanation reaction, this means that the cyclopropylcarbinyl cation must be much more stable than the homoallylic cation. On the basis of these considerations, we decided to investigate the reaction of silyl enol ether **31** with MeMgI (Scheme 7). Since the silyloxy group at C7 would both increase the electron density of the double bond in the homoallylic cation **32** and effectively stabilize the cyclopropylcarbinyl cation **33**, rearrangement of **31** to the normarasmane ketone **34** was expected to be the preferred pathway. Addition of MeMgI to ketone **34** should then lead to the final product in this one-pot operation, the marasmane alcohol **35**. An additional advantage of this approach is the relatively simple synthesis of silyl enol ether **31**.

The synthesis of **31** started with allylic oxidation of the known olefin **28**[7e] using CrO_3−pyridine complex[23] as oxidant. The resulting enone **29** was converted via a five-step reaction sequence to mesylate **30** in 68% overall yield.[11] Reaction of **30** with TMSI and HMDS[24] completed the synthesis of silyl enol ether **31**. When **31** was treated with 5 equiv of MeMgI at room temperature, a fast reaction took place resulting in a ca. 3:2:5 mixture of ketone **34**, the expected alcohol **35**, and the trimethylsilyl

(16) The C7 epimer of **17** refused to give **18**.
(17) Ireland, R. E.; Pfister, G. *Tetrahedron Lett.* **1969**, 2145.
(18) Dihydroxylation reactions on **20** with a catalytic amount of *highly toxic* OsO_4 and an amine oxide as the stoichiometric oxidant were less successful.
(19) Gerdes, H.; Javeri, S.; Marschall, H. *Chem. Ber.* **1980**, *113*, 1907. (b) Kawana, M.; Koresawa, T.; Kuzuhara, H. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1095.
(20) The identity of **9** was tentatively assigned by ^{1}H NMR spectral comparison with **14**.
(21) Place, P.; Roumestant, M.-L.; Gore, J. *Bull. Soc. Chim. Fr.* **1976**, 169.
(22) Orru, R. V. A.; Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; de Groot, A. *J. Org. Chem.* **1993**, *58*, 1199.
(23) Dauben, W. G.; Lorber, M.; Fullerton, D. S. *J. Org. Chem.* **1969**, *34*, 3587.
(24) Miller, R. D.; McKean, D. R. *Synthesis* **1979**, 730.

Scheme 7



ether of **35**, respectively, in 80% yield. A NOE difference experiment on **34** in which selective irradiation of H-9α at δ 1.11 resulted in positive enhancements of the H-5 (δ 1.91), H-1 (δ 2.09), and H-6α (δ 2.21) signals was in agreement with the assigned stereochemistry. The isolation of **34** in this reaction with MeMgI indicates that enolization competes seriously with addition, probably as a result of steric hindrance. The orientation of the Me group at C7 in **35** could not be established by NMR analysis, but was assumed to be α for steric reasons.[25] Methylation of cation **33** or, alternatively, silylation of **35** by TMSI generated in this reaction might explain the formation of the trimethylsilyl ether of **35**. The formation of only rearrangement−cyclopropanation products in this reaction confirmed our hypothesis that the intermediacy of the very stable oxonium ion in combination with an enhanced electron density of the double bond is required for a successful tandem reaction leading to the marasmane skeleton.

A selective formation of ketone **34** could be achieved in 73% yield on exposure of **31** to MgI_2[26] in the presence of HMDS.[27] Subsequent reaction of **34** with MeMgCl then yielded the desired marasmane alcohol **35** (61%) as a single compound. Deprotonation of **34** with KHMDS[28] followed by addition of *N*-phenyltrifluoromethanesulfonimide (Tf_2NPh) afforded enol triflate **36** which was

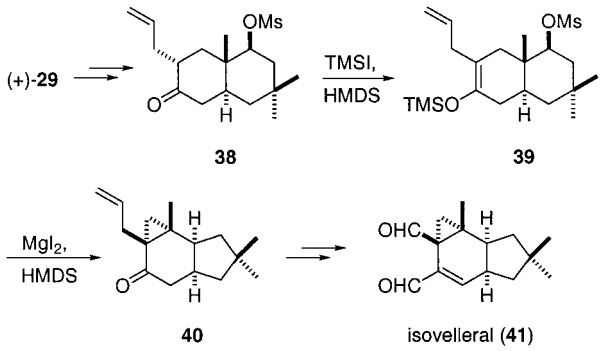
(25) Inspection of a molecular model of **34** indicated that the β direction of approach is strongly shielded.

(26) MgI_2 should be added quickly to avoid air contact as much as possible. Prolonged air contact will lead to inactivity of the reagent.

(27) Without HMDS, the yield of **34** was much lower as a result of cyclopropane ring opening.

(28) LDA, normally used in this reaction, gave only a poor yield of **36**.

Scheme 8



methylated with Me_2CuLi[29] to provide another simple marasmane derivative, olefin **37**, in 40% overall yield.

Application was next extended to the synthesis of the naturally occurring marasmane (+)-isovelleral (**41**).[30] To date, two total syntheses of this strongly antifungal and antibacterial dialdehyde with pungent taste were reported. In Heathcock's racemic approach,[31] the Corey−Chaykovsky reagent was employed to introduce the cyclopropane ring, whereas Wickberg[32] used methylcyclopropenyllithium in his asymmetric synthesis. In our synthetic approach toward isovelleral, cyclopropane ring formation proceeds intramolecularly (Scheme 8). As starting material, we selected optically active mesylate **38** with an allyl group at C8. After conversion of **38** to silyl enol ether **39**, the key step in our approach, the MgI_2-induced rearrangement−cyclopropanation reaction of **39**, should then lead to ketone **40**. It is noteworthy that initial efforts to synthesize the corresponding silyl enol ethers with an ester[33] or a protected carbinol function at C8, failed. With **40** in hand, completion of the synthesis of (+)-isovelleral (**41**) was planned through conversion of the allyl substituent to an aldehyde group[34] and introduction of the second aldehyde group at C7 via a Pd-catalyzed one-carbon homologation.[31]

Mesylate **38** was prepared from optically pure (+)-**29**[35] via a reaction sequence similar to that employed for the synthesis of **30**.[11] Treatment of **38** with TMSI and HMDS gave a high yield[36] of crude **39** which was immediately used in the next reaction with MgI_2, providing the tricyclic ketone **40** in ca. 50% overall yield from (+)-**29**. All the NMR spectroscopic data collected for **40** are consistent with the assigned structure.

Having accomplished the successful rearrangement to **40**, its conversion to (+)-isovelleral was first tried as outlined in Scheme 9. Isomerization of the double bond in **40** with $RhCl_3$ in the presence of K_2CO_3[37] furnished **42** as a 10:1 mixture of *E* and *Z* isomers, respectively, in

(29) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1980**, *21*, 4313.

(30) Hansson, T.; Sterner, O.; Wickberg, B. *J. Org. Chem.* **1992**, *57*, 3822.

(31) Thompson, S. K.; Heathcock, C. H. *J. Org. Chem.* **1992**, *57*, 5979.

(32) Bergman, R.; Hansson, T.; Sterner, O.; Wickberg, B. *J. Chem. Soc., Chem. Commun.* **1990**, 865.

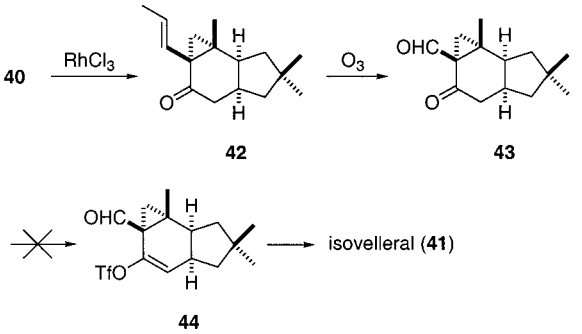
(33) A successful rearrangement−cyclopropanation of a silyl enol ether with a Me ester at C8 would lead directly to a known intermediate in the synthesis of racemic isovelleral. See ref 31.

(34) Hanselmann, R.; Benn, M. *Synth. Commun.* **1996**, *26*, 945.

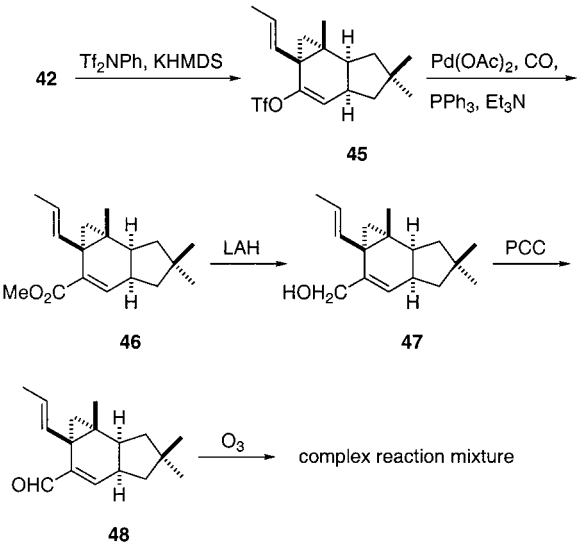
(35) The starting material for the synthesis of (+)-**29**, optically pure (+)-(1*S*,8a*S*)-1,2,3,4,6,7,8,8a-octahydro-3,3,8a-trimethyl-1-naphthalenol, was prepared as previously described. See: Franssen, M. C. R.; Jongejan, H.; Kooijman, H.; Spek, A. L.; Bell, R. P. L.; Wijnberg, J. B. P. A.; de Groot, A. *Tetrahedron: Asymm.* **1999**, *10*, 2729.

(36) Purification by column chromatography resulted in a modest yield (45%) of **39**.

Scheme 9



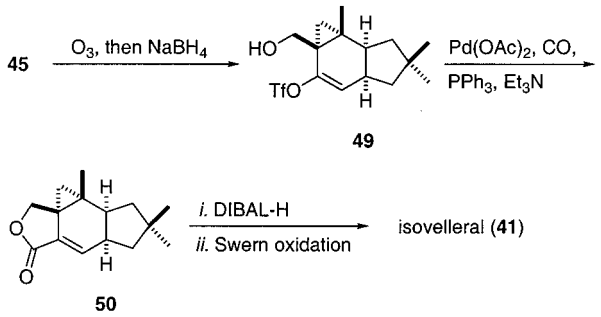
Scheme 10



77% yield. However, the following two steps proved to be more problematic than expected. Ozonolysis of **42**[38] furnished aldehyde (+)-**43** only in poor yield (26%),[39] whereas conversion of **43** to enol triflate **44** as substrate for the one-carbon homologation failed to give any product, probably due to the internal chelation of the enolate function with the aldehyde moiety.[40] The reversed sequence, one-carbon homologation prior to ozonolysis, initially gave more promising results. Enol triflate formation with **42** proceeded now without difficulties and gave **45** in 94% yield (Scheme 10). Pd-catalyzed one-carbon homologation of **45** resulted in a 86% yield of a ca. 4:1 mixture of the α,*β*-unsaturated Me ester **46** and the corresponding acid,[41] respectively. Reduction of this mixture with LAH afforded alcohol **47** as the sole product in almost quantitative yield. Oxidation of **47** with PCC[42] resulted in aldehyde **48**, but subsequent ozonolysis of **48** failed. Ozonolysis of ester **46** gave a similar negative result. In both cases, these failures were explained by interference of the proximate carbonyl function at C7.[43]

Completion of the synthesis of isovelleral could be achieved by following the reaction sequence shown in

Scheme 11



Scheme 11. Ozonolysis of **45** and reduction with $NaBH_4$ furnished, after purification, alcohol **49** in 39% yield.[44] Due to lack of starting material **45**, improvement of the yield of alcohol **49** could not be investigated further, but the results clearly showed that selective ozonolysis of an alkyl-substituted double bond was possible in the presence of an enol triflate double bond.

With **49** in hand, completion of the synthesis of (+)-isovelleral (**41**) involved the Pd-catalyzed one-carbon homologation of **49** to give lactone **50** in 85% yield. Reduction of **50** with excess of DIBAL-H and subsequent Swern oxidation completed the synthesis of (+)-isovelleral. The $[\alpha]^{20}_D$ value of +234° measured for our sample of isovelleral in $CHCl_3$ matched very well with the value of +251° reported for natural isovelleral isolated from *Lactarius vellereus*.[30]

In summary, this novel tandem rearrangement−cyclopropanation approach presents an attractive route to the marasmane framework. The stereocontrolled total synthesis of (+)-isovelleral in 12 steps and ca. 10% overall yield from optically active (+)-**29** shows that this strategy is a useful alternative for the synthesis of complex marasmane sesquiterpenes.

Experimental Section

General Methods. Unless stated otherwise, all reactions were carried out in oven-dried glassware under dry N_2 atmosphere. Solvents were dried by appropriate methods wherever needed. All organic extracts were dried over anhydrous $MgSO_4$. Flash chromatography was performed on 230−400 mesh silica gel. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or benzene-d_6 at 200 and 50 MHz, respectively, unless otherwise noted. Chemical shifts are reported in ppm (δ) relative to $CHCl_3$ (δ 7.24) or benzene (δ 7.15). Optical rotations were taken at 20 °C. IR spectra were recorded as $CHCl_3$ solutions. Mass spectra were determined at 70 eV in the electron impact mode.

Materials. Reagents were purchased from commercial suppliers and used without further purification. The compounds **10**, **16**, and **28** were prepared as previously described.[7e] The ^1H NMR assignments reported for the key compounds **14** and **34** are based on 2D NMR methods (HETCOR, COSY, and NOESY) and NOE difference experiments. (+)-Isovelleral (**41**) was characterized before.[30,31]

Treatment of 12 with Li(O*t*-Bu)$_3$AlH. To a solution of 68.4 mg (0.23 mmol) of **12** in 10 mL of degassed benzene was

(37) Nakamura, H.; Arata, K.; Wakamatsu, T.; Ban, Y.; Shibasaki, M. *Chem. Pharm. Bull.* **1990**, *38*, 2435.

(38) This and following reactions on **42** were carried out with the pure *E* isomer.

(39) Opening of the cyclopropane ring during purification by column chromatography was probably responsible for the modest yield of **43**.

(40) In contrast to **43**, enol triflate formation proceeded smoothly with the compound possessing an ester group instead of an aldehyde function at C8. See ref 31.

(41) The formation of carboxylic acid was explained by the use of not completely dry DMF and/or MeOH in this reaction.

(42) The use of PCC resulted in a modest yield (25%) of **48**. Swern oxidation of **47** may give a better result. See ref 31.

(43) Wu, H.-J.; Lin, C.-C. *J. Org. Chem.* **1996**, *61*, 3820. (b) Wu, H.-J.; Chern, J.-H.; Wu, C.-Y. *Tetrahedron* **1997**, *53*, 2401.

(44) This ozonolysis procedure applied on **45** also produced a diastereometric mixture (12%) of two cross ozonides as was deduced from the ^1H NMR spectrum showing two three-proton doublets at δ 1.26 and 1.31, a two-proton quartet at δ 5.11, and two one-proton singlets at δ 5.06 and 5.19. For example, see: Griesbaum, K.; Bandyopadhyay, A. R.; Meister, M. *Can. J. Chem.* **1986**, *64*, 1553.

added 0.144 g (0.57 mmol) of Li(O*t*-Bu)$_3$AlH. The reaction mixture was refluxed for 22 h under Ar, cooled to room temperature, and then quenched with 1 mL of saturated aqueous Na_2SO_4. After 5 min of vigorous stirring, the reaction mixture was diluted with ether, dried, and evaporated. The remaining residue was flash chromatographed [5:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 16.8 mg (36%) of (1a*S**,2*R**,-3a*R**,6a*S**,6b*S**)-2,5,5,6b-tetramethyloctahydrocyclopropa[*e*]-inden-3(1*H*)-one (**14**) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.08 (dd, J = 5.5, 4.8 Hz, H-9α), 0.33 (ddd, J = 8.3, 5.5, 1.3 Hz, H-9β), 0.94 (s, 3H), 1.00 (dddd, J = 8.3, 4.8, 3.0, 1.3 Hz, H-8), 1.05 (s, 3H), 1.06 (s, 3H), 1.06 (d, J = 6.5 Hz, 3H), 1.36 (dd, J = 13.1, 8.5 Hz, H-4β), 1.53 (dd, J = 12.3, 12.3 Hz, H-2β), 1.75 (ddd, J = 13.1, 9.4, 2.3 Hz, H-4α), 1.81 (ddd, J = 12.3, 6.8, 2.3 Hz, H-2α), 2.62 (ddd, J = 9.8, 9.4, 8.5 Hz, H-5), 2.78 (dddd, J = 12.3, 9.8, 6.8, 1.3 Hz, H-1), 3.03 (qdd, J = 6.5, 3.0, 1.3 Hz, H-7); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.21, 15.24, 18.64, 24.28, 27.21, 27.32, 29.79, 38.76, 40.37, 45.43, 46.04, 48.33, 49.84, 216.23; HRMS calcd for $C_{14}H_{22}O$ (M^+) 206.1671, found 206.1670.

Treatment of 13 with Li(O*t*-Bu)$_3$AlH. Alcohol **13** (0.113 g, 0.37 mmol) was treated with Li(O*t*-Bu)$_3$AlH (0.237 g, 0.93 mmol) for 1.75 h as described above for **12**. Workup and flash chromatography [5:1 petroleum ether (bp 40−60 °C)/EtOAc] gave 51.9 mg (67%) of (1*R**,2*S**,6*R**,7*R**)-1,4,4,8-tetramethyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-8-ene (**15**) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.85 (s, 3H), 1.01 (s, 3H), 1.16 (m, 1H), 1.23 (s, 3H), 1.30−1.39 (m, 2H), 1.54 (ddd, J = 11.7, 7.8, 2.0 Hz, 1H), 1.63 (br s, 3H), 1.81 (dm, J = 17.6 Hz, 1H), 2.29 (dm, J = 17.6 Hz, 1H), 2.41 (app q, J = 8.8 Hz, 1H), 2.71 (dt, J = 10.2, 8.3 Hz, 1H), 3.74 (s, 1H), 5.13 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 19.32, 22.97, 26.00, 28.30, 40.77, 41.36, 42.94, 46.25, 52.16, 54.83, 79.42, 81.12, 116.27, 139.79; HRMS calcd for $C_{14}H_{22}O$ (M^+) 206.1671, found 206.1673.

Treatment of 6 with Li(O*t*-Bu)$_3$AlH. A solution of **6** (35.8 mg, 0.11 mmol) in 5 mL of degassed toluene was treated with Li(O*t*-Bu)$_3$AlH (46.0 mg, 0.18 mmol) at 100 °C for 6 h as described above for **12**. Workup afforded 23.4 mg (97%) of a light yellow oil which, according to GCMS analysis, consisted of **22** (55%), **9** (11%), and at least four other compounds. Careful flash chromatography [10:1 petroleum ether (bp 40−60 °C)/EtOAc] provided 3.8 mg (15%) of almost pure (3a*R**,8*S**,-8a*R**)-2,2,5,6,8-pentamethyl-2,3,3a,7,8,8a-hexahydro-4(1*H*)-azulenone (**22**): ^{1}H NMR (benzene-d_6) δ 0.72 (d, J = 6.5 Hz, 3H), 0.93 (s, 3H), 1.07 (app t, J = 12.5 Hz, 1H), 1.21−1.43 (m, 3H), 1.26 (s, 3H), 1.46 (br s, 3H), 1.72−2.06 (m, 3H), 1.84 (br s, 3H), 2.56 (dd, J = 13.4, 4.6 Hz, 1H), 2.99 (ddd, J = 9.9, 8.3, 4.6 Hz, 1H); ^{13}C NMR (100 MHz, benzene-d_6) δ 16.27, 22.36 (2C), 30.00, 30.32, 37.70, 38.34, 41.07, 46.85, 47.03, 50.86, 55.64, 133.92, 144.32, 205.21; HRMS calcd for $C_{15}H_{24}O$ (M^+) 220.1827, found 220.1824.

Treatment of 6 with MeMgI. To a stirring solution of 20.6 mg (65 μmol) of **6** in 5 mL of degassed toluene at room temperature was added MeMgI (0.2 mL of 0.8 M in ether). After 1.25 h, the reaction mixture was quenched with brine and diluted with ether. The organic phase was washed with brine, dried, and evaporated. The remaining residue was flash chromatographed [5:1 petroleum ether (bp 40−60 °C)/EtOAc] to afford, in order of elution, 0.8 mg (6%) of **9** (GC purity ≈ 90%) and 12.7 mg (56%) of **24**, both as colorless oils. (1a*S**,2*R**,-3a*R**,6a*S**,6b*S**)-1a,2,5,5,6b-Pentamethyloctahydrocyclopropa[*e*]inden-3(1*H*)-one (**9**): IR ($CHCl_3$) 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.01 (dd, J = 5.6, 1.8 Hz, 1H), 0.28 (d, J = 5.6 Hz, 1H), 0.83−1.45 (m, 3H), 0.93 (s, 3H), 1.05 (s, 3H), 1.08 (d, J = 6.6 Hz, 3H), 1.11 (s, 3H), 1.13 (s, 3H), 1.60−1.90 (m, 2H), 2.60−2.85 (m, 2H); MS m/z 220 (M^+). (1*S**,4a*S**,5*S**,8a*R**)-5-Iodo-2,3,4a,7,7-pentamethyl-1,4,4a,5,6,7,8,8a-octahydro-1-naphthalenol (**24**): ^{1}H NMR ($CDCl_3$) δ 0.86 (s, 3H), 0.94 (s, 3H), 0.95 (s, 3H), 1.12−1.26 (m, 2H), 1.25 (br s, OH), 1.51−1.79 (m, 3H), 1.62 (br s, 3H), 1.68 (br s, 3H), 1.98 (ddd, J = 13.4, 4.3, 2.1 Hz, 1H), 2.14 (app t, J = 13.2 Hz, 1H), 3.51 (br s, 1H; becomes br d, J = 8.6 Hz, with D_2O added), 4.41 (dd, J = 13.0, 4.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.34, 14.40, 19.59, 25.22, 32.60, 35.21, 37.82, 38.52, 44.93, 49.22, 49.40, 49.60, 75.66, 126.85, 128.20; HRMS calcd for $C_{15}H_{25}IO$ (M^+) 348.0950, found 348.0948.

Treatment of 12 with MeMgI. Mesylate **12** (39.1 mg, 0.13 mmol) was treated with MeMgI (0.5 mL of 1 M in ether) for 35 min as described above for **6**. Workup and flash chromatography [10:1 to 5:1 petroleum ether (bp 40−60 °C)/EtOAc] gave, in order of elution, 6.0 mg (22%) of **14** and 13.3 mg (31%) of (1*S**,4a*S**,5*S**,8a*R**)-5-iodo-2,4a,7,7-tetramethyl-1,4,-4a,5,6,7,8,8a-octahydro-1-naphthalenol as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.89 (s, 3H), 0.95 (s, 3H), 0.96 (s, 3H), 1.20 (m, 1H), 1.42 (br s, OH), 1.62 (ddd, J = 12.5, 9.0, 3.5 Hz, 1H), 1.73 (br s, 3H), 1.74−1.82 (m, 2H), 1.94 (m, 1H), 2.02 (dd, J = 4.4, 2.1 Hz, 1H), 2.15 (app t, J = 13.1 Hz, 1H), 3.55 (br d, J = 9.0 Hz, 1H), 4.42 (dd, J = 13.1, 4.3 Hz, 1H) 5.38 (br d, J = 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.36, 19.08, 25.16, 32.53, 35.09, 37.64, 39.19, 43.04, 44.68, 49.14, 49.44, 74.27, 122.66, 134.80; HRMS calcd for $C_{14}H_{23}IO$ (M^+) 334.0786, found 334.0770.

Treatment of 25 with MeMgI. Tosylate **25** (11.7 mg, 28.8 μmol) was treated with MeMgI (0.2 mL of 0.8 M in ether) for 40 min as described above for **6**. Workup gave (1*R**,2*S**,-6*R**,7*R**)-1,4,4,8,9-pentamethyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-8-ene (**27**) as a light yellow oil in quantitative yield.[45] Flash chromatography [20:1 petroleum ether (bp 40−60 °C)/EtOAc] provided a pure sample: ^{1}H NMR ($CDCl_3$) δ 0.85 (s, 3H), 1.02 (s, 3H), 1.15 (dd, J = 11.5, 10.6 Hz, 1H), 1.25 (s, 3H), 1.29−1.41 (m, 3H), 1.51 (br s, 3H), 1.60 (br s, 3H), 1.70 (br AB$_d$, J = 17.5 Hz, 1H), 2.25 (br AB$_d$, J = 17.5 Hz, 1H), 2.38 (app q, J = 8.9 Hz, 1H), 2.66 (dt, J = 10.2, 8.4 Hz, 1H), 3.74 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 15.06, 17.50, 23.00, 26.07, 28.34, 41.44, 43.00, 46.33, 46.43, 52.15, 54.44, 80.24, 81.91, 121.63, 131.66; HRMS calcd for $C_{15}H_{24}O$ (M^+) 220.1827, found 220.1829.

Treatment of 31 with MeMgI. A solution of 28.5 mg (76.2 μmol) of **31** in 5 mL of degassed toluene was treated with MeMgI for 30 min as described above for **6**. Workup and flash chromatography [5:1 petroleum ether (bp 40−60 °C)/EtOAc] gave 8.8 mg of an oil which, according to ^{1}H NMR and GC analysis, contained ca. 60% of the trimethylsilyl ether of **35**: ^{1}H NMR (main peaks, benzene-d_6) δ −0.08 (d, J = 4.6 Hz, 1H), 0.20 (s, 9H), 0.43 (d, J = 4.6 Hz, 1H), 1.10 (s, 3H), 1.18 (s, 3H), 1.21 (s, 3H), 1.25 (s, 3 H), 1.37 (s, 3H), 2.48 (dt, J = 6.8, 11.2 Hz, 1H); MS m/z 294 (M^+). Further elution afforded 3.9 mg (25%) of **34** and 2.9 mg (17%) of **35**. The spectroscopic data of **34** and **35** are shown below.

Treatment of 31 with MgI$_2$ and HMDS. To a stirring solution of 63.6 mg (0.17 mmol) of **31** and 180 μL (0.85 mmol) of HMDS in 5 mL of degassed toluene at room temperature was added 70.0 mg (0.25 mmol) of MgI_2. After 2 h, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ and diluted with ether. The organic phase was washed with 1 M aqueous HCl and brine, dried, and evaporated. The remaining residue was flash chromatographed [20:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 25.6 mg (73%) of (1a*R**,3a*S**,6a*S**,-6b*R**)-1a,5,5,6b-tetramethyloctahydrocyclopropa[*e*]inden-2(1*H*)-one (**34**) as a colorless oil: ^{1}H NMR (400 MHz, benzene-d_6) δ 0.30 (d, J = 4.9 Hz, H-9β), 0.82 (s, 3H), 0.91 (s, 6H), 1.00 (dd, J = 13.3, 3.4 Hz, 1H), 1.02 (app t, J = 12.6 Hz, 1H), 1.11 (d, J = 4.9 Hz, H-9α), 1.32 (s, 3H), 1.39 (dd, J = 13.3, 6.9 Hz, 1H), 1.44 (dd, J = 12.6, 6.6 Hz, 1H), 1.88 (dd, J = 19.1, 6.4 Hz, H-6β), 1.91 (m, H-5), 2.09 (ddd, J = 12.6, 6.9, 6.6 Hz, H-1), 2.21 (dd, J = 19.1, 11.5 Hz, H-6α); ^{13}C NMR (100 MHz, benzene-d_6) δ 14.49, 20.63, 28.40, 30.81, 31.40, 32.77, 34.87, 36.09, 37.44, 40.75, 43.71, 45.84, 49.57, 208.50; HRMS calcd for $C_{14}H_{22}O$ (M^+) 206.1671, found 206.1673.

(1a*R,2*R**,3a*S**,6a*S**,6b*R**)-1a,2,5,5,6b-Pentamethyldecahydrocyclopropa[*e*]inden-2-ol (35).** To a stirring solution of 24.3 mg (0.12 mmol) of **34** in 5 mL of THF at room temperature was added MeMgCl (0.1 mL of 3 M in THF). After 1.25 and 4.25 h, two other 0.1 mL-portions of MeMgCl were added. The reaction mixture was stirred at room temperature for an additional 4 h, quenched with saturated aqueous NH_4-

(45) GC analysis revealed the presence (ca. 15%) of another, unknown product.

Cl, and diluted with ether. The organic phase was washed with brine, dried, and evaporated to give an oily residue which was flash chromatographed on basic alumina [10:1 petroleum ether (bp 40−60 °C)/EtOAc] to afford 16.1 mg (61%) of **35** as a colorless oil:^{1}H NMR (benzene-d_6) δ −0.10 (d, J = 4.6 Hz, 1H), 0.47 (d, J = 4.6 Hz, 1H), 0.75 (br s, OH), 0.90 (m, 1H), 0.92 (s, 3H), 1.05 (s, 3H), 1.11 (s, 6H), 1.12 (s, 3H), 1.19 (dd, J = 14.8, 2.2 Hz, 1H), 1.40 (dd, J = 14.8, 8.3 Hz, 1H), 1.55−1.62 (m, 2H), 1.73 (dd, J = 12.2, 9.8 Hz, 1H), 2.05 (m, 1H), 2.44 (dt, J = 8.3, 10.9, 1H); ^{13}C NMR (100 MHz, benzene-d_6) δ 14.88, 22.21, 23.82, 25.21, 27.22, 29.26, 29.46, 29.90, 32.01, 37.96, 39.50, 42.00, 48.39, 50.95, 73.54; HRMS calcd for $C_{15}H_{26}O$ (M^+) 222.1984, found 222.1982.

(1a*R,3a*R**,6a*S**,6b*R**)-1a,5,5,6b-Tetramethyl-1,1a,-3a,4,5,6,6a,6b-octahydrocyclopropa[*e*]inden-2-yl Trifluoromethanesulfonate (36).** To a solution of 10.0 mg (48.5 μmol) of **34** and 87.0 mg (0.24 mmol) of Tf_2NPh in 1.5 mL of 2:1 THF/toluene, cooled to −78 °C, was added KHMDS (0.5 mL of 0.5 M in toluene). After being stirred at −78 °C for 2 h, the reaction mixture was quenched with brine and diluted with ether. The organic phase was washed with brine, dried, and evaporated. The remaining residue was flash chromatographed [7:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 11.0 mg (67%) of **36** as a colorless oil: ^{1}H NMR (benzene-d_6) δ 0.22 (d, J = 4.7 Hz, 1H), 0.84 (s, 6H), 0.94 (s, 3H), 1.00−1.49 (m, 5H), 1.15 (s, 3H), 1.92−2.07 (m, 2H), 5.05 (d, J = 1.7 Hz, 1H); ^{13}C NMR (benzene-d_6) δ 14.32, 20.36, 20.72, 27.53, 29.00, 31.48, 31.68, 37.32, 37.63, 41.98, 45.19, 47.66, 116.69, 118.69 (q, $J_{C,F}$ = 320 Hz), 151.63; HRMS calcd for $C_{15}H_{21}F_3O_3S$ (M^+) 338.1164, found 338.1161.

(1a*S,3a*S**,6a*S**,6b*R**)-1a,2,5,5,6b-Pentamethyl-1,1a,-3a,4,5,6,6a,6b-octahydrocyclopropa[*e*]indene (37).** MeLi (0.55 mL of 1.6 M in ether) was added to a stirring suspension of 0.107 g (0.56 mmol) of CuI in 2 mL of THF at −10 °C. The mixture was stirred at −10 °C for 45 min, and then a solution of 18.9 mg (56 μmol) of **36** in 1 mL of THF was added via cannula. The reaction mixture was allowed to warm to 0 °C, stirred for an additional 75 min, and quenched with saturated aqueous NH_4Cl. After dilution with ether, the organic phase was washed with saturated aqueous NH_4Cl and brine, dried, and evaporated. The remaining residue was flash chromatographed (pentane) to give 6.8 mg (60%) of **37** as a colorless oil: ^{1}H NMR (benzene-d_6) δ 0.26 (d, J = 3.6 Hz, 1H), 0.91 (d, J = 3.6 Hz, 1H), 1.01 (s, 3H), 1.09 (s, 3H), 1.14 (s, 6H), 1.32 (dd, J = 13.0, 1.4 Hz, 1H), 1.40 (app t, J = 11.9 Hz, 1H), 1.60 (m, 1H), 1.68 (dd, J = 13.0, 7.7 Hz, 1H), 1.81 (br s, 3H), 2.30−2.38 (m, 2H), 4.86 (br s, 1H); ^{13}C NMR (benzene-d_6) δ 17.20, 21.16, 21.66, 22.14, 25.73, 29.14, 32.03, 32.25, 37.69, 38.97, 43.69, 45.59, 48.82, 123.22, 137.72; HRMS calcd for $C_{15}H_{24}$ (M^+) 204.1878, found 204.1876.

(1a*R*,3a*S*,6a*S*,6b*R*)-1a-Allyl-5,5,6b-trimethyloctahydrocyclopropa[*e*]inden-2(1*H*)-one (40). To a solution of **38** (0.560 g, 1.29 mmol) in 10 mL of CH_2Cl_2 at room temperature were added 0.69 mL (3.25 mmol) of HMDS and 0.37 mL (2.60 mmol) of TMSI. The reaction mixture was stirred for 35 min and, after addition of saturated aqueous $NaHCO_3$, diluted with ether. The two-phase system was separated, and the organic layer was washed with saturated aqueous $Na_2S_2O_3$ and brine. Drying and evaporation gave an oily residue (0.537 g) which was treated with MgI_2 and HMDS for 1.5 h as described above for **31**. Workup and flash chromatography [10:1 petroleum ether (bp 40−60 °C)/EtOAc] gave 0.247 g (82%) of **40** as a colorless oil: $[\alpha]^{20}_D$ = −29° (*c* 1.85, $CHCl_3$); ^{1}H NMR (benzene-d_6) δ 0.37 (d, J = 5.0 Hz, 1H), 0.82 (s, 3H), 0.91 (s, 3H), 0.94 (m, 1H), 0.96 (s, 3H), 1.01 (d, J = 5.0 Hz, 1H), 1.12 (app t, J = 12.5 Hz, 1H), 1.37 (dd, J = 13.3, 6.7 Hz, 1H), 1.47 (dd, J = 12.5, 6.5 Hz, 1H), 1.75−2.26 (m, 5H), 2.84 (dd, J = 14.9, 6.7 Hz, 1H), 5.02 (br d, J = 10.2 Hz, 1H), 5.07 (br d, J = 17.0 Hz, 1H), 6.07 (ddt, J = 17.0, 10.2, 6.6 Hz, 1H); ^{13}C NMR (benzene-d_6) δ 20.60, 26.30, 30.91, 31.42, 32.40, 33.31, 35.56, 37.20, 38.80, 40.85, 43.44, 45.32, 48.98, 115.63, 137.45, 207.50; HRMS calcd for $C_{16}H_{24}O$ (M^+) 232.1827, found 232.1824.

(1a*S*,3a*S*,6a*S*,6b*R*)-5,5,6b-Trimethyl-1a-[(1-propenyl]-octahydrocyclopropa[*e*]inden-2(1*H*)-one (42). A mixture of 36.8 mg (159 μmol) of **40**, 4.7 mg (18 μmol) of $RhCl_3 \cdot H_2O$, and 22.0 mg (159 μmol) of K_2CO_3 in 2 mL of EtOH was heated at 60 °C for 2 h. Upon cooling to room temperature, ether was added, and the organic phase was washed with brine, dried, and evaporated. The remaining residue was flash chromatographed [5:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 28.3 mg (76%) of **42** as a 10:1 mixture of *E* and *Z* isomers, respectively. Repeated flash chromatography [5:1 petroleum ether (bp 40−60 °C)/EtOAc] gave the *E* isomer in pure form along with an almost pure sample of the *Z* isomer. *E* isomer: $[\alpha]^{20}_D$ = +20° (*c* 1.16, $CHCl_3$); ^{1}H NMR (400 MHz, benzene-d_6) δ 0.82 (s, 3H), 0.90 (s, 3H), 0.90 (d, J = 5.2 Hz, 1H), 0.93 (s, 3H), 1.05 (dd, J = 13.2, 3.8 Hz, 1H), 1.11 (app t, J = 12.5 Hz, 1H), 1.14 (d, J = 5.2 Hz, 1H), 1.41 (ddd, J = 13.2, 7.3, 0.8 Hz, 1H), 1.48 (dd, J = 12.5, 6.6 Hz, 1H), 1.65 (dd, J = 6.5, 1,6 Hz, 3H), 1.89−1.99 (m, 2H), 2.16 (dt, J = 12.4, 7.0 Hz, 1H), 2.23 (m, 1H), 5.31 (dq, J = 15.5, 6.5 Hz, 1H), 6.09 (dd, J = 15.5, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, benzene-d_6) δ 18.20, 20.54, 24.79, 30.60, 31.22, 35.79, 36.45, 37.42, 41.37, 42.12, 43.30, 45.90, 49.73, 127.40, 127.62, 206.98; HRMS calcd for $C_{16}H_{24}O$ (M^+) 232.1827, found 232.1825. *Z* isomer: ^{1}H NMR (benzene-d_6) δ 0.58 (d, J = 4.8 Hz, 1H), 0.83 (s, 3H), 0.93 (s, 3H), 0.96 (s, 3H), 0.99−1.53 (m, 4H), 1.28 (d, J = 4.8 Hz, 1H), 1.63 (br d, J = 6.8 Hz, 3H), 1.69−2.03 (m, 2H), 2.05−2.41 (m, 2H), 5.40 (br d, J = 10.6 Hz, 1H), 5.80 (dq, J = 10.6, 6.8 Hz, 1H); ^{13}C NMR (benzene-d_6) δ 14.78, 21.25, 28.68, 30.68, 31.42, 33.19, 35.87, 37.27, 38.36, 40.87, 42.91, 45.27, 48.97, 126.97, 131.26, 204.76; HRMS calcd for $C_{16}H_{24}O$ (M^+) 232.1827, found 232.1825.

(1a*S*,3a*R*,6a*S*,6b*R*)-5,5,6b-Trimethyl-1a-[(1*E*)-1-propenyl]-1,1a,3a,4,5,6,6a,6b-octahydrocyclopropa[*e*]inden-2-yl Trifluoromethanesulfonate (45). To a solution of 66.6 mg (287 μmol) of **42** (*E* isomer) and 205.0 mg (573 μmol) of Tf_2NPh in 5 mL of THF, cooled to −78 °C, was added KHMDS (1.15 mL of 0.5 M in toluene). After being stirred at −78 °C for 1 h, the reaction mixture was quenched with brine, allowed to come to room temperature, and diluted with ether. The organic layer was washed with brine, dried, and evaporated. The remaining residue was flash chromatographed [10:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 98.4 mg (94%) of **45** as a colorless oil: $[\alpha]^{20}_D$ = −37° (*c* 0.51, $CHCl_3$); ^{1}H NMR (benzene-d_6) δ 0.82 (d, J = 4.8 Hz, 1H), 0.84 (s, 3H), 0.86 (s, 3H), 0.93 (d, J = 4.8 Hz, 1H), 0.95 (s, 3H), 1.07 (dd, J = 13.3, 1.4 Hz, 1H), 1.22 (m, 1H), 1.39−1.52 (m, 2H), 1.60 (dd, J = 3.5, 1.2 Hz, 3H), 1.95−2.10 (m, 2H), 5.08 (br s, 1H), 5.40−5.51 (m, 2H); ^{13}C NMR (benzene-d_6) δ 17.68, 20.59, 26.65, 28.89, 29.46, 31.50, 31.75, 37.34, 37.78, 41.12, 45.15, 47.65, 116.96, 119.20 (q, $J_{C,F}$ = 320 Hz), 125.99, 131.75, 150.47; HRMS calcd for $C_{17}H_{23}F_3O_3S$ (M^+) 364.1320, found 364.1321.

(1a*R*,3a*R*,6a*S*,6b*R*)-1a-(Hydroxymethyl)-5,5,6b-trimethyl-1,1a,3a,4,5,6,6a,6b-octahydrocyclopropa[*e*]inden-2-yl Trifluoromethanesulfonate (49). A solution of 34.1 mg (94 μmol) of **45** in 5 mL of CH_2Cl_2 was cooled to −78 °C, and O_3 was bubbled through the solution until the solution turned faintly blue. Dry N_2 was then bubbled through the stirring solution until the blue color disappeared, and at that moment a few drops of DMS were added.[46] After 10 min, 18.5 mg of $NaBH_4$ (0.49 mmol) and 5 mL of MeOH were added, and the reaction mixture was allowed to come to room temperature and stirred for 40 min. The reaction mixture was then quenched with 1 M aqueous HCl and diluted with ether. The organic layer was washed with brine, dried, and evaporated. The remaining residue was flash chromatographed [3:1 petroleum ether (bp 40−60 °C)/EtOAc] to afford 12.9 mg (39%) of **49** as a colorless oil: $[\alpha]^{20}_D$ = −31° (*c* 0.25, $CHCl_3$); ^{1}H NMR (benzene-d_6) δ 0.34 (d, J = 4.8 Hz, 1H), 0.46 (br s, OH), 0.79 (d, J = 4.8 Hz, 1H), 0.84 (s, 3H), 0.93 (s, 3H), 0.98 (s, 3H), 1.05 (dd, J = 13.3, 1.5 Hz, 1H), 1.36−1.49 (m, 3H), 1.90−2.02 (m, 2H), 2.90 (br AB_d, J = 12.1 Hz, 1H), 4.11 (br AB_d, J =

(46) Quenching with DIBAL-H instead of DMS gave **49** (35%) along with some impure aldehyde **44**: ^{1}H NMR (major peaks, benzene-d_6) δ 0.76 (s, 3H), 0.84 (s, 3H), 0.85 (s, 3H), 5.10 (d, J = 2.2 Hz, 1H), 9.60 (s, 1H). Reduction of the impure fraction containing **44** with $NaBH_4$ gave another portion of **49** through which the total yield of **49** in this two-step reaction amounted to 50%.

12.1 Hz, 1H), 5.15 (br s, 1H); ^{13}C NMR (benzene-d_6) δ 20.24, 26.65, 28.03, 28.13, 31.60 (2C), 37.41, 37.52, 41.49, 45.01, 47.62, 61.15, 118.29, 119.18 (q, $J_{C,F}$ = 320 Hz), 150.01; HRMS calcd for $C_{15}H_{21}F_3O_4S$ (M^+) 354.1113, found 354.1112.

(1a*S*,5a*S*,8a*S*,8b*R*)-7,7,8b-Trimethyl-5a,6,7,8,8a,8b-hexahydrocyclopropa[4,5]indeno[5,6-*c*]furan-4(1*H*)-one (50). Enol triflate **49** (10.4 mg, 29 μmol) was treated with a mixture of MeOH, Et_3N, Ph_3P, and $Pd(OAc)_2$ in DMF under a CO atmosphere for 3.5 h as described for **45**.[11] Workup and flash chromatography [3:1 petroleum ether (bp 40−60 °C)/EtOAc] gave 5.8 mg (85%) of **50** as a white solid: $[\alpha]^{20}_D = -16°$ (*c* 0.29, $CHCl_3$); ^{1}H NMR (400 MHz, benzene-d_6) δ 0.66 (s, 3H), 0.68 (d, J = 4.5 Hz, 1H), 0.80−0.86 (m, 2H), 0.82 (s, 3H), 0.83 (s, 3H), 1.14 (dd, J = 13.4, 1.7 Hz, 1H), 1.21 (m, 1H), 1.48 (dd, J = 13.4, 8.4 Hz, 1H), 1.95−2.06 (m, 2H), 3.64 (AB_d, J = 8.8 Hz, 1H), 3.82 (AB_d, J = 8.8 Hz, 1H), 6.18 (d, J = 2.1 Hz, 1H); ^{13}C NMR (100 MHz, benzene-d_6) δ 19.07, 24.97, 26.76, 26.95, 31.70, 31.84, 37.56, 40.12, 42.28, 44.57, 47.30, 69.89, 130.20, 133.50, 168.82; HRMS calcd for $C_{15}H_{20}O_2$ (M^+) 232.1463, found 232.1463.

(+)-Isovelleral (41). To a solution of 5.8 mg (25 μmol) of **50** in 2 mL of ether, cooled to −78 °C, was added DIBAL-H (125 μL of 1 M in hexane). The solution was stirred at −78 °C for 15 min and then allowed to warm to room temperature. Another 50 μL of DIBAL-H was added, and stirring was continued for an additional 25 min. The reaction mixture was quenched with 1 M aqueous HCl, diluted with ether, and washed with brine. The organic layer was dried and evaporated to give 5.6 mg of ((1a*S*,3a*S*,6a*S*,6b*R*)-2-(hydroxymethyl)-5,5,6b-trimethyl-3a,4,5,6,6a,6b-hexahydrocyclopropa[*e*]inden-1a(1*H*)-yl)methanol as a white solid: HRMS calcd for $C_{15}H_{24}O_2$ (M^+) 236.1776, found 236.1782. The NMR data were identical with those reported in the literature.[31] This diol (5.6 mg) was oxidized with oxalyl chloride and DMSO as described.[31] Workup and flash chromatography [5:1 petroleum ether (bp 40−60 °C)/EtOAc] afforded 3.2 mg (55%) of **41** as a white solid: $[\alpha]^{20}_D = +234°$ (*c* 0.16, $CHCl_3$) (lit.[30] $[\alpha]^{20}_D = +251°$); HRMS calcd for $C_{15}H_{20}O_2$ (M^+) 232.1463, found 232.1464. The NMR data were identical with those reported in the literature. [31]

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Supporting Information Available: Experimental details for the preparation of **6**, **11**−**13**, **17**−**21**, **25**, **29**−**31**, **38**, **39**, **43**, and **46**−**48**. ^{1}H NMR spectra for all new compounds and ^{1}H-coupled ^{13}C NMR spectrum of **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

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