Total Synthesis of (±)-Tremulenolide A and (±)-Tremulenediol A via a Stereoselective Cyclopropanation/Cope Rearrangement Annulation Strategy

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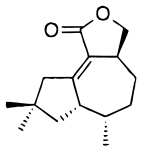
Received August 25, 1997

Short total syntheses of (±)-tremulenolide A (**1**) and (±)-tremulenediol A (**2**) are described. The critical step is a dirhodium tetracarboxylate-catalyzed tandem cyclopropanation/Cope rearrangement between the vinyldiazoacetate **4** and the 2(*Z*),4(*E*)-hexadiene **5**. This step results in full control of the relative stereochemistry at the three stereogenic centers that exist in the natural products. Due to problems with alkene face selectivity, the approach was not amenable to an efficient asymmetric synthesis of **1** and **2**.

The tremulanes represent a new class of sesquiterpene metabolites isolated from a fungal pathogen of the quaking aspen.[1] Two examples of these compounds are tremulenolide A (**1**) and tremulenediol A (**2**). We have recently developed a method for the stereoselective synthesis of seven-membered rings by a tandem cyclopropanation/Cope rearrangement between vinylcarbenoids and dienes.[2] In this paper, we describe the utilization of this chemistry in a short, highly stereoselective synthesis of **1** and **2**.[3]



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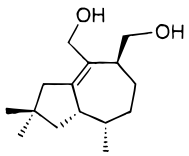

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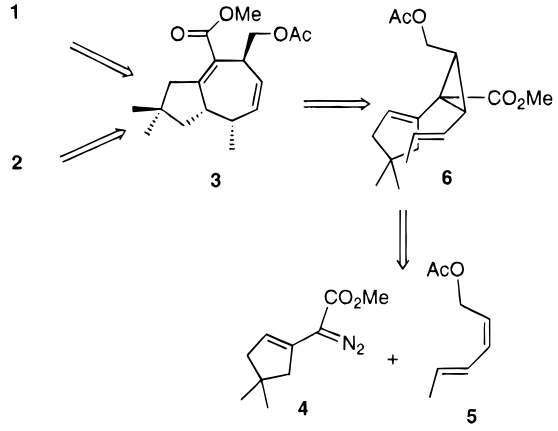
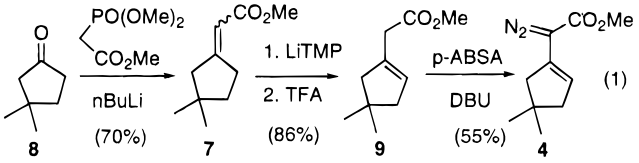
The general strategy for the utilization of the tandem cyclopropanation/Cope rearrangement for the synthesis of **1** and **2** is summarized in Scheme 1.[4] Both **1** and **2** would be derived from the cycloheptadiene **3**, which in turn, would be derived from the vinyldiazoacetate **4** and the diene **5**. Due to the requirement of a boat transition state for the Cope rearrangement of the divinylcyclopropane intermediate **6**, the three stereogenic centers in **3** would be formed with complete control of relative stereochemistry.[2,5] The success of the scheme depends on the remarkable stereoselectivity of vinylcarbenoid cyclopropanations that strongly favors the formation of *cis*-divinylcyclopropanes in the reaction with dienes.[2] Furthermore, the approach would highlight the subtle regioselectivity of vinylcarbenoid cyclopropanations, where efficient intermolecular cyclopropantions occur with 1,2-*cis*-disubstituted alkenes but do not occur with 1,2-*trans* disubstituted alkenes.[2,4,6]

Scheme 1



The vinyldiazoacetate **4** was prepared as outlined in eq 1.[3b] The unsaturated ester **7** was readily prepared from the cyclopentanone **8**[7] in 70% yield by a Horner−Emmons reaction. The direct diazotization of **7** using



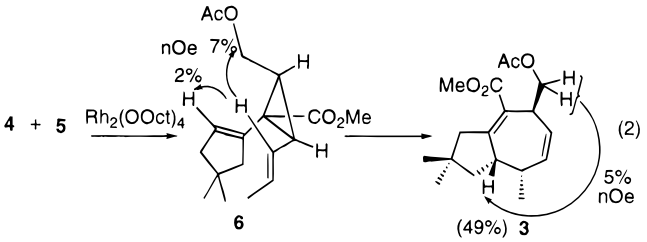
LDA and tosyl azide proceeded in low yield and with poor regiocontrol. A successful alternate strategy to **4** was to deconjugate **7** regioselectively by treatment with lithium tetramethylpiperidide at −94 °C followed by an acid quench to form **9** in 86% yield, contaminated with only a trace (~5%) of the other possible regioisomer. A diazo-transfer reaction on **9** using *p*-acetamidobenzenesulfonyl azide (*p*-ABSA)[8] and DBU at 45 °C resulted in

(1) Ayer, W. A.; Cruz, E. R. *J. Org. Chem.* **1993**, *58*, 7529.
(2) Davies, H. M. L. *Tetrahedron* **1993**, *49*, 5203.
(3) For recent synthetic studies of compounds related to the tremulanes, see: (a) Habeck, T.; Wolff, C.; Tochtermann, W. *Tetrahedron Lett.* **1995**, *36*, 2041. (b) Davies, H. M. L.; Doan, B. D. *Tetrahedron Lett.* **1996**, *37*, 3967.
(4) For examples of the use of the Cope rearrangement of divinylcyclopropanes for the synthesis of pseudoguaianes, see: (a) Marino, J. P.; Kaneko, T. *J. Org. Chem.* **1974**, *39*, 3175. (b) Marino, J. P.; Browne, L. J. *Tetrahedron Lett.* **1976**, 3245. (c) Wender, P. A.; Eissenstat, M. A.; Filosa, M. P. *J. Am. Chem. Soc.* **1979**, *101*, 2196. (d) Wender, P. A.; Filosa, M. P. *J. Org. Chem.* **1976**, *41*, 3490. (e) Piers, E.; Nagakura, I. *Tetrahedron Lett.* **1976**, 3237. (f) Piers, E.; Morton, H. E.; Nagakura, I.; Thies, R. W. *Can. J. Chem.* **1983**, *61*, 1226.
(5) Hudlicky, T.; Fan, R.; Reed, J. W.; Gadamasetti, K. G. *Org. React.* **1992**, *41*, 2.
(6) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. K.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6897−6909
(7) Fairlie, D. P.; Bosnich, B. *Organometallics* **1988**, *7*, 936.
(8) Davies, H. M. L.; Cantrell, W. R.; Romines, K. R.; Baum, J. S. *Org. Synth.* **1991**, *70*, 93.

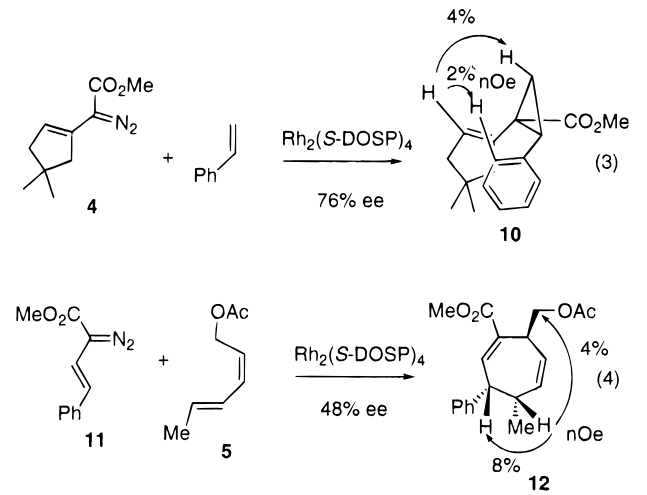
S0022-3263(97)01577-6 CCC: $15.00
Published on Web 01/14/1998

the formation of **4** in 55% yield. The *E*,*Z*-diene **5** was prepared by acylation of the corresponding alcohol.[3b,9,10]

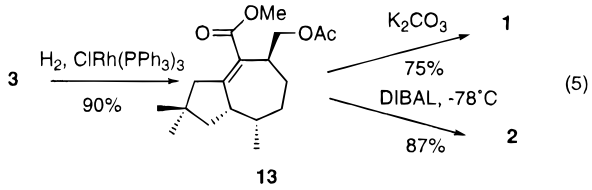
Rhodium(II) octanoate-catalyzed decomposition of the vinyldiazoacetate **4** in the presence of a 12-fold excess of diene **5** in refluxing hexane resulted in the formation of a mixture of the desired product **3** and the *cis*-divinylcyclopropane **6** (eq 2). Confirmation that the divinylcyclopropane was indeed the cis isomer **6** was obtained by NOE difference analysis. Generally, the Cope rearrangement of divinylcyclopropanes occurs at or below ambient temperatures.[2] In the case of **6**, a crowded boat transition state is required for the Cope rearrangement. Thus, forcing conditions are necessary to induce the rearrangement in this system.[11] This was achieved by Kugelrohr distillation under vacuum of the crude material at 60 °C, to recover the diene, and then at 140 °C, to obtain the cycloheptadiene **3** as a single regioisomer in 49% yield with full control of relative stereochemistry. Supporting evidence that **3** had the predicted stereochemistry was obtained by NOE difference analysis, which showed a large enhancement between the bridgehead proton and the protons α to the acetate.



The next series of reactions explored the possibility of an asymmetric entry into the tremulane skeleton. We have recently described that rhodium(II) (*S*)-*N*-[*p*-(dodecylphenyl)sulfonyl]prolinate [Rh_2(*S*-DOSP)$_4$] is a highly effective chiral catalyst for asymmetric cyclopropanations by vinylcarbenoids.[6] It was expected that the utilization of Rh_2(*S*-DOSP)$_4$ for the conversion of **4** and **5** to **6** would result in a highly enantioselective entry to **3**. In practice, this was not the case, as the reaction with Rh_2(*S*-DOSP)$_4$ resulted in the formation of **3** in only 4% ee. To probe if the low enantioselectivity is due to poor face selectivity at the carbenoid or the diene, we have carried out the test reactions shown in eqs 3 and 4. Decomposition of the vinyldiazoacetate **4** in the presence of styrene in refluxing hexanes resulted in the formation of the cyclopropane **10** in 76% ee (eq 3). This result demonstrates that Rh_2(*S*-DOSP)$_4$ is capable of inducing efficient face selectivity in the reaction of the carbenoid derived from **4**. Decomposition of the vinyldiazoacetate **11** in the presence of the diene **5** in refluxing hexanes resulted in the formation of the cycloheptadiene **12** in 48% ee (eq 4). Since our earlier studies have shown that the vinylcarbenoid derived from **11** undergoes a highly enantioselective cyclopropanation with styrene (86% ee in refluxing hexanes, 98% ee at −78 °C)[6] and a range of other dienes,[12] it is likely that the low enantioselectivity observed in eq 4 is due to lack of face selectivity on the diene.



Completion of the synthesis of **1** and **2** was carried out as outlined in eq 5. The *cis*-olefin in the intermediate **3** was selectively hydrogenated by Wilkinson's catalyst to form **13** in 90% yield.[3b] Hydrolysis of the acetyl group by aqueous potassium carbonate followed by lactonization resulted in the formation of (±)-tremulenolide A (**1**) in 75% yield. Alternatively, reduction of the two ester groups in **13** with DIBAL resulted in the formation of (±)-tremulenediol A (**2**) in 87% yield. The spectral data for **1** and **2** were consistent with the literature data.[1]



The excellent diastereocontrol but poor enantiocontrol that is observed in the cyclopropanation of the diene **5** can be rationalized by the model that we have proposed for the asymmetric cyclopropanation by Rh_2(*S*-DOSP)$_4$.[6] In this model, the catalyst is considered to behave as if it has D_2 symmetry, and the rhodium−carbenoid complex can be represented as shown in Figure 1.[6] The cyclopropanation is considered to be nonsynchronous with the alkene approaching in a side-on approach.[6] In the case of the diene, from an electronic viewpoint, approach according to structure A would be preferred, while from a steric viewpoint, attack according to structure B would be preferred. Both orientations would form *cis*-divinylcyclopropanes, but the divinylcyclopropanes would have opposite absolute stereochemistry (**6** and *ent*-**6**). We have previously seen in the reaction of vinylcarbenoids with pyrroles that steric influences can dominate over electronic effects in the regioselectivity of vinylcarbenoid cyclopropanations.[13] In the case of the diene **5**, we would propose that the electronic and steric effects are fairly evenly balanced such that they cancel each other out, leading to product with low asymmetric induction.

In summary, the tandem cyclopropanation/Cope rearrangement sequence results in a rapid entry to two

(9) (a) Furber, M.; Herbert, J. M.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1* **1989**, 683. (b) Paquette, L. A.; Crouse, G. D.; Sharma, A. K. *J. Am. Chem. Soc.* **1982**, *104*, 4411.

(10) Vasil'ev, A. A.; Poddubnaya, S. S.; Cherkaev, G. V.; Cherkaev, V. G. *Zh. Org. Khim.* **1987**, *23*, 1622.

(11) For examples of the effect of steric hindrance on the rate of the Cope rearrangement of divinylcyclopropanes, see: (a) Schneider, M. P.; Rau, A. *J. Am. Chem. Soc.* **1979**, *101*, 4426. (b) Cantrell, W. R., Jr.; Davies, H. M. L. *J. Org. Chem.* **1991**, *56*, 723.

(12) (a) Davies, H. M. L.; Peng, Z.-Q.; Houser, J. H. *Tetrahedron Lett.* **1994**, *35*, 8939. (b) Davies, H, M, L.; Stafford, D. G.; Doan, B. D.; Houser, J. H. *J. Am. Chem. Soc.*, submitted.

(13) Davies, H. M. L.; Matasi. J. J.; Hodges, L. M.; Huby, N. J. S.; Thornley, C.; Kong, N.; Houser, J. H. *J. Org. Chem.* **1997**, *62*, 1095.

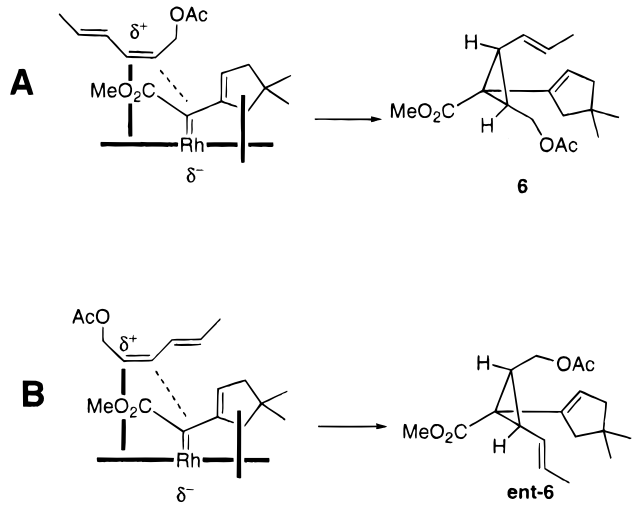


Figure 1.

members of the tremulane sesquiterpenes. The approach results in excellent control of relative stereochemistry at the three stereogenic centers, but due to problems with alkene face selectivity, the approach was not amenable to an efficient asymmetric synthesis.

Experimental Section

General Procedures. All reactions were run in oven-dried glassware under argon. Reagents were reagent-grade materials and used as obtained unless noted. THF and hexanes were distilled over sodium/benzophenone prior to use. 2,2,6,6-tetramethylpiperidine, CH_3CN, and CH_2Cl_2 were distilled over CaH_2 prior to use. 3,3-Dimethylcyclopentanone (**8**),[7] methyl 2-diazo-4-phenylbutenoate (**11**),[6] Rh_2(*S*-DOSP)$_4$,[6] and *p*-ABSA[8] were prepared according to procedures described in the literature. 1-Acetoxy-(2*Z*,4*E*)-2,4-hexadiene (**5**)[10] was prepared by acetylation of the corresponding alcohol.[9]

^{1}H NMR spectra were run at 200, 300, 400, or 500 MHz, and ^{13}C NMR spectra were recorded at 75 MHz using $CDCl_3$ as solvent. ^{13}C DEPT experiments were run at 75 MHz. Chemical shifts are reported in ppm downfield from TMS. IR spectra were recorded using a Nicolet Impact 420 FTIR. Column chromatography was carried out on silica gel 60, 230−400 mesh. Hydrogenations were carried out on a Parr hydrogenation apparatus.

Methyl 3,3-Dimethylcyclopentylidineacetate (7) *n*-BuLi (53.52 mL, 2.5 M in hexane, 133 mmol) was added to a solution of trimethylphosphonoacetate (25.6 g, 140 mmol) in THF (125 mL) at −78 °C. A solution of **8** (15.0 g, 133 mmol) in THF (25 mL) was added quickly, and the mixture was stirred at −78 °C for 6 h and then at ambient temperature for 4 h. Water was added, and the mixture was extracted with ether. The combined extracts were rinsed with brine, dried (Na_2SO_4), and concentrated. Purification by distillation (Kugelrohr, 35−60 °C, 1.5 mmHg) gave a mixture of *E*/*Z* isomers (1:1) of **7** as a clear colorless oil: 15.65 g (70%); IR (neat) 2955, 1717, 1660 cm^{-1}; ^{1}H NMR (300 MHz) δ 5.73 (br s, 2 H), 3.64 (s, 6 H), 2.82 and 2.52 (2 t, J = 7.7 Hz, 4 H), 2.57 and 2.21 (2 s, 4 H), 1.54 and 1.46 (2 t, J = 7.5 Hz, 4 H), 0.99 and 0.86 (2 s, 12 H). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.39; H, 9.62.

Methyl 4,4-Dimethyl-1-cyclopentylacetate (9). *n*-BuLi (23.8 mL, 2.5 M in hexane, 59.5 mmol) was added to a solution of 2,2,6,6-tetramethylpiperidine (10.2 mL, 60.1 mmol) in THF (150 mL) at 0 °C under argon. After 20 min, the solution was cooled to −94 °C and HMPA (10.3 mL, 59.5 mmol) was added. A cold (−94 °C) solution of **7** (5.00 g, 29.8 mmol) in THF (50 mL) was added after 30 min. The solution was stirred for 40 min and then was poured over a cold (−94 °C) solution of CF_3CO_2H (10 mL) in THF (50 mL). Water was added, and the mixture was extracted with ether. The extracts were rinsed with aqueous $NaHCO_3$, water, and brine and then dried (Na_2SO_4). Concentration and distillation (Kugelrohr, 40−60 °C, 1.5 mmHg) gave **9** as a slightly amber oil: 4.28 g (86%); IR (neat) 2950, 1731 cm^{-1}; ^{1}H NMR (300 MHz) δ 5.34 (s, 1 H), 3.66 (s, 3 H), 3.06 (s, 2 H), 2.11 (br s, 4 H), 1.05 (s, 6 H) ^{13}C NMR (75 MHz) δ 172.2, 135.3, 127.1, 51.5, 50.1, 47.6, 38.7, 37.0, 29.6. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.40; H, 9.65.

Methyl 4,4-Dimethyl-1-cyclopentenyldiazoacetate (4). A solution of **9** (3.26 g, 19 mmol) in CH_3CN (30 mL) was added by cannula to dry *p*-ABSA (5.60 g, 23 mmol), and the solution was then stirred at room temperature. A solution of DBU (8.90 g, 58 mmol) in CH_3CN (30 mL) was added by cannula. The resulting yellow solution was warmed to 45 °C and stirred for 4 h. *CAUTION: As this reaction involved heating an azide, it was conducted behind a polycarbonate blast shield. It should be noted, however, that shock sensitivity studies have shown that p-ABSA does not have explosive properties, and we have never experienced any problems using this reagent.* The reaction mixture was quenched with saturated NH_4Cl and extracted into ether. The organic extracts were rinsed with brine, dried (Na_2SO_4), and concentrated. The residue was triturated with petroleum ether/ether (30:1), and the resulting solution was concentrated and purified by chromatography using petroleum ether/ether (30:1) as eluent to give **4** as an orange oil: 2.05 g (55%); IR (neat) 2950, 2927, 2838, 2088, 1704, 1621, 1450 cm^{-1}; ^{1}H NMR (300 MHz) δ 5.78 (br s, 1 H), 3.76 (s, 3 H), 2.22 (br s, 4 H), 1.06 (s, 6 H); ^{13}C NMR (75 MHz) δ 166.2, 135.2, 123.0, 122.9, 122.6, 51.7, 48.8, 48.3, 38.3, 37.9, 32.5, 29.6, 28.5. Due to the relative instability of the diazo compound, elemental analysis was not attempted.

Methyl (5α,8β,8aα)-5-(Acetoxymethyl)-1,2,3,5,8,8a-hexahydroazuleno-4-carboxylate (3). A solution of **4** (93 mg, 0.48 mmol) in hexanes (10 mL) was added dropwise over 30 min to a stirred solution of $Rh_2(OOct)_4$ (5 mg, 6.4×10^{-3} mmol) and **5** (0.80 g, 5.7 mmol) in hexanes (10 mL), heated under reflux. The reaction mixture was concentrated, and the residue was distilled (kugelrohr) to give recovered diene **5** (60 °C, 1−2 mmHg) and the crude product (140 °C, 1−2 mmHg). Purification by chromatography using petroleum ether/ether (5:1) gave **3** as a white solid: 72 mg (49%); mp 63−65 °C; IR 2952, 1744, 1713, 1645 cm^{-1}; ^{1}H NMR (500 MHz) δ 5.82 (ddd, J = 11.9, 6.2, 1.2 Hz, 1 H), 5.43 (dd, J = 11.9, 6.7 Hz, 1 H), 4.27 (dd, J = 9.5, 6.3 Hz, 1 H), 4.25 (dd J = 9.5, 6.4 Hz, 1 H), 3.70 (s, 3 H), 3.66 (ddd, J = 6.7, 6.4, 6.3 Hz, 1 H), 3.56 (m, 1 H), 2.81 (dd, J = 16.8, 2.1 Hz, 1 H), 2.23 (d, J = 16.8 Hz, 1 H), 2.13 (m, 1 H), 2.02 (s, 3 H), 1.58 (ddd, J = 12.5, 8.5, 2.1 Hz, 1 H), 1.38 (dd, J = 12.5, 9.8 Hz, 1 H), 1.11 (s, 3 H), 0.88 (d, J = 7 Hz, 3 H), 0.84 (s, 3 H); ^{13}C NMR (75 MHz) δ 171.0 (C═O), 168.5 (C═O), 165.19 (q), 137.1 (CH), 125.6 (CH), 123.5 (q), 67.12 (CH_2), 51.3 (CH_2), 51.3 (CH_3), 46.1 (CH), 43.5 (CH_2), 40.5 (C−H), 38.1 (q), 34.5 (CH_2), 28.3 (CH_3), 27.45 (CH_3), 21.0 (CH_3), 14.6 (CH_3); MS *m*/*z* 246 (100), 234 (32), 233 (82), 232 (41), 231 (22), 201 (18), 187 (38), 173 (61), 131 (19), 129 (28). Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.62; H, 8.57. The % ee for the reaction using Rh_2(*S*-DOSP)$_4$ was determined by HPLC using a Chiracel OD column (25 × 0.46 cm, 0.5% 2-PrOH in hexane, UV 255 nm, 1 mL/min), t_R = 9.1 min (minor), 9.8 min (major), 4% ee.

Methyl 2β-Phenyl-1β-(4,4-dimethyl-1-cyclopenten-1-yl)cyclopropane-1-carboxylate (10). A solution of **4** (98 mg, 0.5 mmol) in hexane (5 mL) was added dropwize to a stirred solution of Rh_2(*S*-DOSP)$_4$ (0.95 mg, 5.0×10^{-3} mmol) and styrene (0.70 mL, 5.0 mmol) in hexane (5 mL), heated under reflux. The mixture was then concentrated, and the residue was purified by chromatography using petroleum ether/ether (4:1) to give **10** as a colorless oil: 100.2 mg (76%); IR (neat) 2943, 1723, 1500 cm^{-1}; ^{1}H NMR (500 MHz) δ 7.24−7.18 (m, 4 H), 7.11 (d, J = 7.0 Hz, 1 H), 5.42 (br s, 1 H), 3.73 (s, 3 H), 2.99 (dd, J = 8.5, 7.5 Hz, 1 H), 2.22 (dd, J = 15.5, 2.0 Hz, 1 H), 2.06 (dd, J = 16.0, 2.5 Hz, 1 H), 1.88 (dd, J = 16.0, 2.5 Hz, 1 H), 1.78−1.75 (m, 2 H), 1.27 (dd, J = 15.5, 2.0 Hz, 1 H), 0.99 (s, 3 H), 0.45 (s, 3 H); ^{13}C NMR (75 MHz) δ 174.1 (C═O), 137.3 (q), 135.8 (q), 129.7 (CH), 128.5 (CH), 127.6 (CH), 126.5 (CH),

52.1 (CH_3), 48.9 (CH_2), 46.9 (CH_2), 38.3 (q), 33.0 (q), 32.4 (CH), 29.6 (CH_3), 29.2 (CH_3), 18.7 (CH_2); MS *m*/*z* 270 (75), 255 (23), 238 (19), 223 (44), 211 (23), 195 (39), 182 (15), 165 (18), 155 (47), 141 (31), 128 (19), 121 (28), 115 (47), 105 (16), 91 (100), 78 (21), 72 (34). Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.89; H, 8.20. 76% ee (determined by ^{1}H NMR using 20 mol % (−)-Pr(hfc)$_3$).

Methyl 7*β*-(Acetoxymethyl)-4α-methyl-3α-phenylcyclohepta-2,5-diene-1-carboxylate (12). A solution of **11** (113.4 mg, 0.561 mmol) in hexanes (10 mL) was added dropwise to a stirred solution of Rh$_2$(*S*-DOSP)$_4$ (10 mg, 5.6×10^{-3} mmol) and **5** (0.32 g, 2.3 mmol) in hexanes (10 mL), heated under reflux. The mixture was concentrated, and the residue was purified by chromatography using petroleum ether/ether (4:1) to give **12** as a clear, slightly yellow oil: 72 mg (41%); IR 2960, 2872, 1750, 1704 cm^{-1}; ^{1}H NMR (500 MHz) δ 7.42 (d, J = 7 Hz, 1 H), 7.35−7.25 (m, 5 H), 5.73−5.66 (m, 2 H), 4.39 (dd, J = 10.5, 6.5 Hz, 1 H), 4.23 (dd, J = 10.5, 6.5 Hz, 1 H), 4.19 (br s, 1 H), 3.93 (q, J = 6.5 Hz, 1 H), 3.76 (s, 3H), 2.74 (bs, 1 H), 2.05 (s, 3 H), 0.95 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz) δ 171.0, 167.9, 146.5, 141.1, 137.8, 131.4, 128.8, 128.3, 126.8, 126.1, 66.11, 52.2, 48.3, 38.3, 37.3, 21.0, 16.5; MS *m*/*z* 314 (M$^+$), 254 (54), 240 (36), 195 (100), 181 (16), 165 (18), 105 (21); HRMS calcd for $C_{19}H_{22}O_4$ 314.1518, found 314.1490. The % ee for the reaction using Rh$_2$(*S*-DOSP)$_4$ was determined by HPLC using a Chiracel OD column (25 × 0.46 cm, 5.0% 2-PrOH in hexane, UV 255 nm, 1 mL/min), t_R = 8.5 min (minor), 10.7 min (major), 48% ee.

Methyl (5α,8*β*,8aα)-5-(Acetoxymethyl)-1,2,3,5,6,7,8,8a-octahydroazuleno-4-carboxylate (13). A solution of **3** (181 mg, 0.59 mmol) and ClRh(PPh$_3$)$_3$ (34 mg, 0.026 mmol) in absolute ethanol (25 mL) was shaken at 40 psi H_2 for 13 h. The mixture was then concentrated and the residue purified by chromatography using petroleum ether/ether (5:1) as eluent to give **13** as a clear film: 165 mg (90%); IR 2950, 1750, 1704, 1647 cm^{-1}; ^{1}H NMR (500 MHz) δ 4.41 (dd, J = 11.0, 10.0 Hz, 1 H), 4.19 (dd, J = 11.0, 6.0 Hz, 1 H), 3.71 (s, 3 H), 3.24 (m, 1 H), 3.18 (m, 1 H), 2.61 (dd, J = 17.0, 2.5 Hz, 1 H), 2.22 (dd, J = 17.0, 2.0 Hz, 1 H), 2.06 (s, 3 H), 1.90 (m, 1 H), 1.80 (bs, 1 H), 1.78 (m, 1 H), 1.68 (m, 1 H), 1.57 (m, 2 H), 1.45 (dd, J = 12.9, 10.8 Hz, 1 H), 1.09 (s, 3 H), 0.85 (d, J = 7.2 Hz, 1 H), 0.82 (s, 3 H); ^{13}C NMR (125 MHz) δ 171.2, 169.8, 162.7, 125.4, 62.2, 51.64, 51.36, 48.2, 44.9, 38.5, 37.3, 31.7, 31.4, 28.4, 26.8, 21.0, 20.6, 11.8; MS *m*/*z* 248 (M − HOAc), 235 (21), 234 (100), 233 (40), 219 (18), 189(16), 173 (10), 119 (11); HRMS calcd for $C_{16}H_{24}O_2$ (M − HOAc) 248.1776, found 248.1760.

(±)-Tremulenolide A (1). A solution of K_2CO_3 (0.42 g, 3.03 mmol) in water (4 mL) and methonol (1 mL) was added to **13** (68.7 mg, 0.223 mmol) in methanol (3 mL) and then stirred for 12 h. CH_2Cl_2 (2 mL) and water (7 mL) were added, and the solution was extracted into ether. The combined extracts were dried over Na_2SO_4, concentrated, and purified by column chromatography using pentane/ether as eluent (2:1) to give **1** as a white solid: 39.1 mg (75%); mp 80−82 °C; IR 2924, 2867, 1755, 1678, 1460 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.33 (dd, J = 8.4, 8.4 Hz, 1 H), 3.61 (dd, J = 10.4, 8.4 Hz, 1 H), 3.19 (m, 1 H), 3.06 (m, 1 H), 2.88 (dd, J = 19.6, 1.2 Hz, 1 H), 2.46 (ddd, J = 19.6, 4.4, 3.2 Hz, 1 H), 2.13−1.9 (m, 2 H), 1.82 (m, 1 H), 1.71 (dddd, J = 1.2, 1.6, 6.4, 7.6 Hz, 1 H), 1.48 (d, J = 10.8 Hz, 1 H), 1.47−1.42 (m, 2 H), 1.11 (s, 3 H), 0.96 (s, 3 H), 0.93 (d, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz) δ 171.0, 161.3, 120.8, 70.8, 48.4, 45.4, 44.9, 41.0, 37.3, 32.9, 32.7, 29.1, 28.1, 27.4, 17.9; MS *m*/*z* 234 (M$^+$), 220 (13), 219 (100); HRMS calcd for $C_{15}H_{22}O_2$ 234.1613, found 234.1625. The spectral data are consistent with the published data.[1]

(±)-Tremulenediol A (2). DIBAL (1.0 M in hexane, 1.8 mL, 1.8 mmol) was added to a solution of **13** (77 mg, 0.25 mmol) in CH_2Cl_2 (5 mL) stirred at −78 °C. The stirred solution warmed to ambient temperature over 9 h. Methanol (0.5 mL) was added, followed by a saturated aqueous solution of sodium potassium tartrate. The organics were extracted with ether, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography using ether as eluent to give **2** as a clear film: 52.2 mg (87%); IR 3286, 2918, 1455 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.21 (d, J = 11.2 Hz, 1 H), 3.99 (dd, J = 10.0, 9.6 Hz, 1 H), 3.81 (d, J = 11.2 Hz, 1 H), 3.59 (dd, J = 9.6, 4.8 Hz, 1 H), 3.07 (dd, J = 9.6, 8.8 Hz, 1 H), 2.63 (bs, 1 H), 2.51 (m, 1 H), 2.26 (dd, J= 14.8, 2.4 Hz, 1 H), 1.9 (d, J = 15.2 Hz, 1 H), 1.83−1.66 (m, 3 H), 1.62−1.54 (m, 3 H), 1.50 (ddd, J = 12.4, 8.4, 2.4 Hz, 1 H), 1.37 (dd, J = 11.6, 11.2 Hz, 1 H), 1.05 (s, 3 H), 0.85 (s, 3 H), 0.81 (d, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz) δ 145.8, 132.3, 65.6, 63.3, 48.0, 46.0, 45.5, 45.3, 37.0, 32.6, 31.6, 28.5, 26.8, 22.5, 11.6. MS *m*/*s* 220 (28), 190 (18), 189 (100), 133 (19), 119 (20), 105 (20), 95 (21), 91 (15), 81 (11), 55 (18); HRMS calcd for $C_{15}H_{26}O_2$ 220.1827 (M − H_2O), found 220.1816. The spectral data are consistent with the published data.[1]

Acknowledgment. Financial support of this work by the National Science Foundation (CHE 9421649) is gratefully acknowledged.

Supporting Information Available: ^{1}H NMR data for (±)-tremulenolide A (**1**) and (±)-tremulenediol A (**2**) (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO971577A