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Toward the Total Synthesis of Vinigrol: Synthesis of epi-C-8-Dihydrovinigrol

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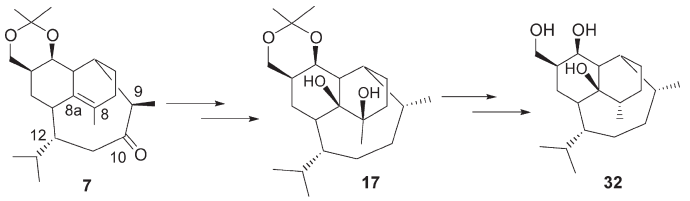

Two approaches to vinigrol starting from the advanced tricyclic core **7** have been explored using as key intermediates epoxide **12** and diol **17**. The preparation of the properly functionalized epoxide **12** has been achieved in a straightforward fashion. However, all attempts to prepare tertiary alcohol **14** by reductive opening of **12** failed. In alternative exploratory efforts to achieve the same goal, allylic alcohols **16** and **29** were prepared by regioselective dehydration of diol **17**. Whereas *endo*-isomer **16** was found to be reluctant to undergo catalytic hydrogenation, the *exo* counterpart **29** led to the undesired isomer affording after hydrolysis epi-C-8-dihydrovinigrol **32**.

Introduction

Vinigrol (**1**, Figure 1) is a novel diterpenoid isolated in 1987 by Hashimoto, Ando, and their colleagues at the Fujisawa Pharmaceutical Co. from *Virgaria nigra* F-5408, a fungus strain found at the foot of Mount Aso in Japan.[1] An evaluation of the biological activity of vinigrol shows promising properties. Very early on, it was demonstrated that this natural product decreased arterial blood pressure in rats in a dose-dependent manner. It also inhibited platelet activating factor and epinephrine induced platelet aggregation.[2] In addition, it was found that **1** is a powerful tumor necrosis factor (TNF) antagonist. Vinigrol may therefore be used to treat endotoxic shock, inflammation, infections, or cachexia or to arrest the progression from AIDS-related complex to AIDS.[3]

Structurally, vinigrol possesses a totally unprecedented decahydro-1,5-butanonaphthalene framework, involving a *cis*-decalin system bridged by an eight-membered ring and features eight contiguous stereocenters. Although **1** is relatively small in size, its congested and rigid structure provides a particularly challenging synthetic problem.

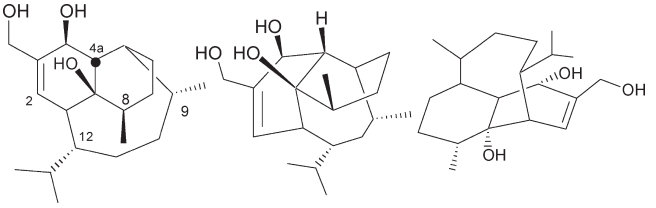

FIGURE 1. Representations of vinigrol (**1**).

(1) Uchida, I.; Ando, T.; Fukami, N.; Yoshida, K.; Hashimoto, M.; Tada, T.; Koda, S; Morimoto, Y. *J. Org. Chem.* **1987**, *52*, 5292.

(2) (a) Ando, T; Tsurumi, Y.; Ohata, N.; Ushida, I.; Hoshida, K.; Okuhara, M. *J. Antibiot.* **1988**, *41*, 25. (b) Ando, T.; Yoshida, K.; Okuhara, M. *J. Antibiot.* **1988**, *41*, 31.

(3) (a) Norris, D. B. ; Depledge, P. ; Jakson, A. P. PCT Int. Appl. WO 9107 953, **1991**. (b) Nakajima, H. ; Yamamoto, N. ; Kaisi, T. Jpn. Kokai Tokyo Koho JP 07206668; *Chem. Abstr.* **1995**, *123*, 246812.

(4) Studies toward vinigrol: (a) For a review, see Tessier, G.; Barriault L. *Org. Prep. Proc. Int.* **2007**, *39*, 311. (b) Mehta, G.; Reddy, K. S. *Synlett* **1996**, 625. (c) Kito, M.; Sakai, T.; Haruta, N.; Shirahama, H.; Matsuda, F. *Synlett* **1996**, 1057. (d) Matsuda, F; Kito, M.; Sakai, T.; Okada, N.; Miyashita, M; Shirahama, H. *Tetrahedron* **1999**, *55*, 14369–14380. (e) Goodman, S. N. Ph.D. Thesis, Harvard University, **2000**. (f) Paquette, L. A.; Guevel, R.; Sakamoto, S.; Kim, I. H.; Crawford, J. *J. Org. Chem.* **2003**, *68*, 6096. (g) Paquette, L. A.; Efremov, I.; Liu, Z. *J. Org. Chem.* **2005**, *70*, 505. (h) Paquette, L. A.; Efremov, I. *J. Org. Chem.* **2005**, *70*, 510. (i) Paquette, L. A.; Liu, Z.; Efremov, I. *J. Org. Chem.* **2005**, *70*, 514. (j) Morency, L.; Barriault, L. *Tetrahedron Lett.* **2004**, *45*, 6105. (k) Morency, L.; Barriault, L. *J. Org. Chem.* **2005**, *70*, 8841. (l) Grise, C. M.; Tessier, G.; Barriault, L. *Org. Lett.* **2007**, *9*, 1545. (m) Souweha, M. S.; Enright, G. D.; Fallis, A. G. *Org. Lett.* **2007**, *9*, 5163. (n) Maimone, T. J.; Voica, A.-F.; Baran, P. S. *Angew. Chem., Int. Ed.* **2008**, *47*, 3054. (p) Morton, J. G. M.; Kwon, L. D.; Freeman, J. D.; Njardarson, J. T. *Synlett* **2009**, 23.

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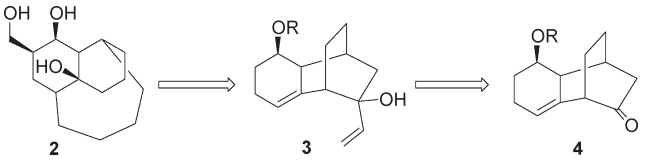
SCHEME 1



As such, it holds a special place alongside other historically challenging diterpene systems such as ingenanes and taxanes.

The unusual structure of this natural product combined with its promising biological properties has attracted significant attention from the synthetic community. As a result, considerable efforts have been devoted toward the synthesis of vinigrol.[4] Despite these efforts, a complete total synthesis of **1** has yet to be reported. From the different published approaches, it was learned that the formation of two of three rings of vinigrol can be achieved without posing serious problems. However, the formation of the third ring, especially the eight-membered ring, is problematic. Variety of approaches reported by Paquette group have demonstrated the difficulty in forming the *ansa* bridge from a pre-existing *cis*-decalin framework.[4f−i] Recently, three successful syntheses of the tricyclic core of vinigrol based on the intramolecular Diels−Alder reaction have been published by research group of Barriault,[4l] Fallis,[4m] and Baran.[4n]

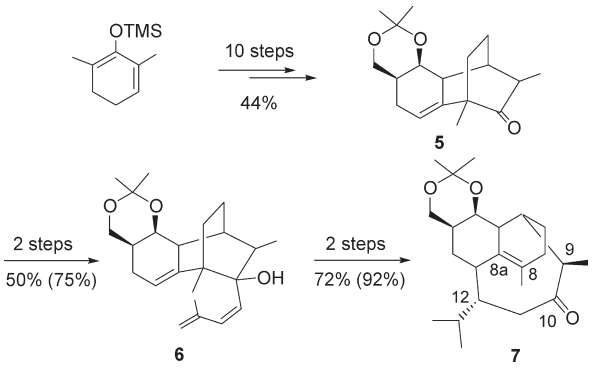
As early as 1993, we reported the successful entry into the functionalized decahydro-1,5-butanonaphthalene ring system of vinigrol in a very concise manner.[5a] Our strategy is based on the recognition that the oxygenated tricyclic skeleton **2** of vinigrol can be quickly elaborated via an anionic oxy-Cope rearrangement of a tricyclic vinyl carbinol such as **3**, which could arise from stereoselective alkylation of enone **4** (Scheme 1).

However, the previously described model was not adequately functionalized for the expeditious completion of the synthesis. In particular, the stereoselective introduction of the isopropyl group at C-12[6] seemed to be a major problem. We disclosed later an efficient 14-step synthesis of the fully elaborated vinigrol carbon skeleton **7**. In this advanced intermediate, methyl groups at C-8 and C-9 were introduced at the first stage and installation of the isopropyl at C-12 was planned before the oxy-Cope rearrangement as outlined in Scheme 2.[5e] We now report our efforts to reach the total synthesis of vinigrol starting from the key intermediate **7**.

Result and Discussion

The previously described tricyclic ketone **7** has the required relative configuration of the isopropyl group at C-12. However, the stereochemistry of methyl group in the eight-membered ring was opposite relative to vinigrol. Therefore, in this phase of the synthesis attention was directed to inversion of C-9 methyl stereochemistry and removal the carbonyl group at C-10. To this end, a three-step protocol consisting on epimerization at the ketone followed by reduction and deoxygenation was first considered. However, all attempts to equilibrate the methyl group under basic or acidic conditions were unsuccessful. Treatment of **7** with LDA at low temperature followed by quench with ammonium chloride or with *t*-BuOK in *t*-BuOH or in toluene at room temperature left the starting material unchanged. At higher temperature (refluxing *t*-BuOH or toluene), an intramolecular oxo-ene cyclization occurred affording **8** in 70% yield. This compound was also obtained by heating **7** in the absence of base, confirming the thermal character of this cyclization.[7] On the other hand, exposure of ketone **7** to 10% aqueous oxalic acid led to oxetane **9** as the result of hydrolysis of the acetal group and the intramolecular reaction between the carbonyl group and the double bond (Scheme 3).

SCHEME 2



Given the tendency of **7** to undergo transannular cyclizations, the removal of carbonyl group at C-10 must be achieved at this stage. To this end, ketone **7** was reduced with $LiAlH_4$ and the resulting alcohol was dehydrated with $POCl_3$ to afford diene **10** (Scheme 4).[8] Treatment of **10** with 1 equiv of *m*-CPBA at 0 °C selectively affected the tetrasubstituted double bond leading to epoxide **11** in 95% yield. Catalytic hydrogenation of the remaining double bond in the presence of 5% rhodium on alumina gave rise to a chromatographically separable 2:1 mixture of **12** (less polar) and its epimer **13** (more polar) in 94% yield.[9] The relative configuration of the methyl group at C-9 in the major isomer **12** was found to be the same compared to that of vinigrol as established by NOESY correlations and confirmed by X-ray crystallographic analysis.[5e]

Having achieved inversion of C-9 methyl stereochemistry and removal the carbonyl group at C-10, the next major goal

(5) (a) Devaux, J.-F; Hanna, I.; Lallemand, J.-Y.; Prangé, T. *J. Org. Chem.* **1993**, *58*, 2349. (b) Devaux, J.-F; Hanna, I.; Lallemand, J.-Y.; Prangé, T. *J. Chem. Res., Synop.* **1996**, 32. (c) Devaux, J.-F; Fraisse, P.; Hanna, I.; Lallemand, J.-Y. *Tetrahedron Lett.* **1997**, *36*, 9471. (d) Devaux, J.-F; Hanna, I.; Lallemand, J.-Y. *J. Org. Chem.* **1997**, *62*, 5062. (e) Gentric, L.; Hanna, I.; Ricard, L . *Org. Lett.* **2003**, *5*, 1139. (f) Gentric, L.; Hanna, I.; Huboux, A.; Zeghdoudi, R. *Org. Lett.* **2003**, *5*, 3631.

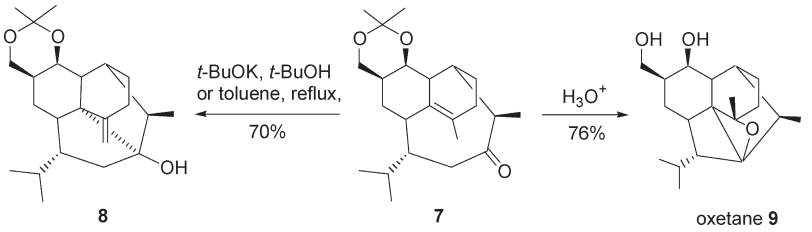
(6) The numbering used in this paper refers to the corresponding centers of vinigrol.

(7) For a review of thermal cyclization of unsaturated ketones see: Conia, J. M.; Le Perchec, P. *Synthesis* **1975**, 1.

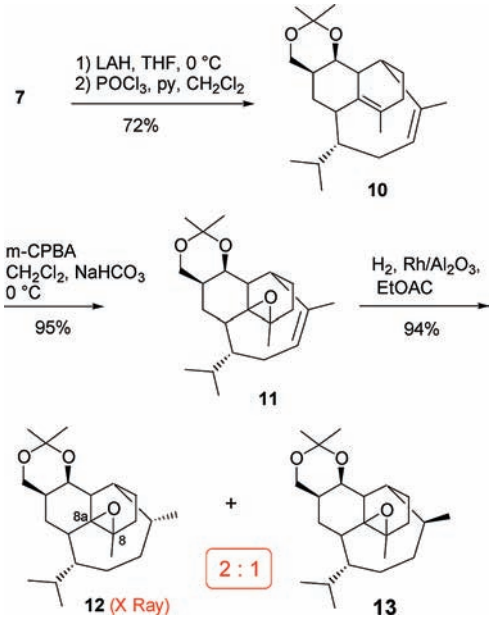
(8) Initial attempts to carry out the epoxidation of the intermediate alcohol failed; the resulting epoxide rapidly underwent an intramolecular ring opening by the hydroxyl group producing the corresponding cyclic ether.

(9) The ratio of **12** and its epimer **13** depends upon the experimental conditions of the hydrogenation and may vary from 2:3 to 2:1. The best result (2:1) was obtained when the reaction mixture was stirred under hydrogen in the presence of a large amount of catalyst for 17 h (see Supporting Information).

SCHEME 3



SCHEME 4

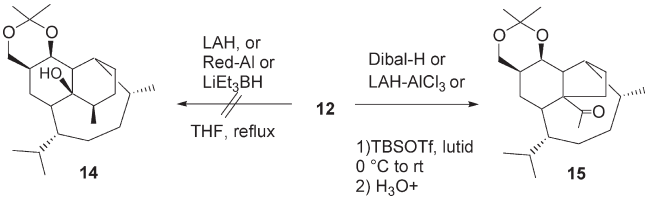


in the synthesis was to obtain alcohol **14**. To this end, reductive cleavage of epoxide **12** was investigated. The various hydride reagents that we chose to employ proved to be uniformly incapable of producing **14**. Exposure of epoxide **12** to $LiAlH_4$, $LiEt_3BH$ (super hydride) or Na Al $H_2(OCH_2CH_2OCH_3)_2$ (Red Al) in refluxing THF for prolonged times left the starting material unchanged. Treatment of **12** with $LiAlH_4-AlCl_3$ or Dibal-H gave a mixture of products from which the rearranged compound **15** was isolated (Scheme 5). This product was cleanly obtained by exposure of **12** to TBSOTf in the presence of lutidine followed by hydrolysis of the resulted silyl enol ether. Recourse to other conventional methods such as dissolved metals (Li, Na, or Ca) in amines (liquid ammonia or ethylenediamine) or Cp2TiCl failed to give the desired product. This unexpected lack of reactivity of epoxide **12** toward reducing reagents may be explained by the steric hindrance around C-8−C-8a bond.

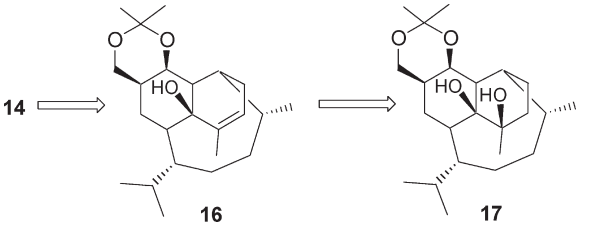
Because our attempts to advance the synthesis of vinigrol by reductive opening of epoxide **12** were not rewarded with success, the deliberate decision was made to consider diol **17** as candidate suitable to our objectives. The perceived practical advantages of this approach included the possible regioselective dehydration of **17** providing alkene **16**, which could be transformed to **14** via catalytic hydrogenation as outlined in Scheme 6.

To prepare **17**, hydration of epoxide **12** was first attempted. However, treatment of **12** with few drops of

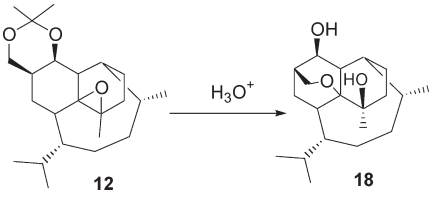
SCHEME 5



SCHEME 6



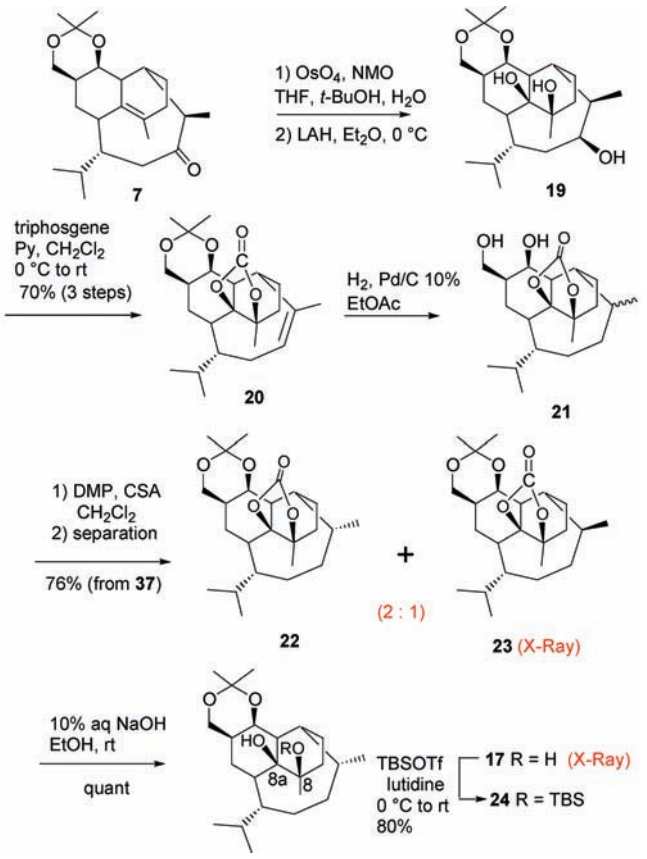
SCHEME 7



aqueous 0.1 N solution of HCl or $HClO_4$ in THF at room temperature furnished **18** (Scheme 7). In this reaction, hydrolysis of the acetonide group occurred first, followed by the intramolecular cleavage of epoxide by the resulting primary alcohol. Other attempts to prepare **17** from **12** were unsuccessful.

Finally, diol **17** was prepared starting from ketone **7** according to the synthetic Scheme 8. Exposure of **7** to osmium tetroxide (50%) in the presence of an excess NMO afforded cyclic osmate diester, which was left unchanged by treatment of the reaction mixture with aqueous sodium hydrogen sulfite solution even upon prolonged times. Therefore, the isolated brown solid osmate was reduced with $LiAlH_4$ furnishing triol **19** almost quantitatively. Treatment of **19** with triphosgene led to cyclic carbonate **20** (70% overall yield from **7**) as a result of protection of the1,2-diol with concomitant dehydration of the secondary alcohol. Catalytic hydrogenation of **20** was first carried on with 5% rhodium on alumina in ethyl acetate. Under these conditions, a chromatographically separable 1:7 mixture of **22** (less polar) and its epimer **23** (more polar) was obtained. The relative configuration of the methyl group

SCHEME 8



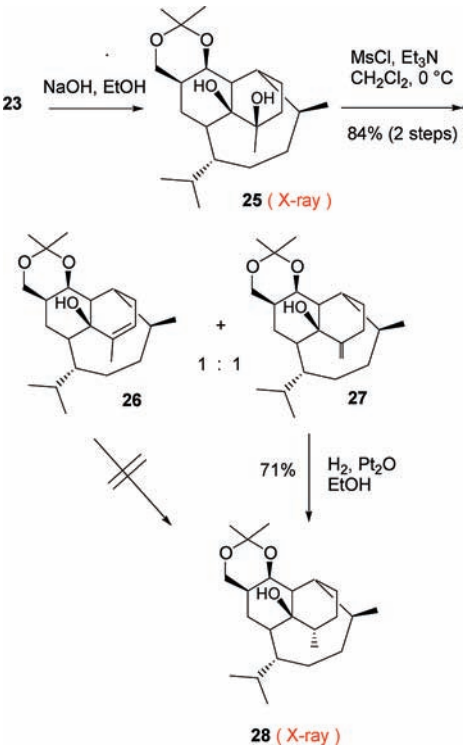
at C-9 in the major isomer **23**, established by X-ray crystallographic analysis, was found to be opposite to that in vinigrol. By contrast, when 10% Pd/C was used instead of 5% Rh/Al_2O_3, the stereochemical outcome of hydrogenation was inversed. Thus, stirring **20** in EtOAc for 24 h in the presence of an excess of 10% Pd/C gave diol **21** as an inseparable mixture of epimers in 2:1 ratio by NMR. Submission of this mixture to 2,2-dimethoxypropane in the presence of catalytic amount of CSA afforded a separable 2:1 mixture of **22** and its epimer **23** in 76% combined yield from **20**.The inversion of the stereoselectivity observed when Pd/C was used may be explained by the presence of hydroxyl groups resulting from hydrolysis of acetonide prior hydrogenation.[10]

It has been known for a long time that polar groups, especially hydroxyl groups, can influence stereochemical outcome of olefin hydrogenation over metals, particularly in rigid systems.[11] To assess this assumption, diol **21** was prepared by acid-catalyzed hydrolysis of **20** and then subjected to hydrogenation over Pd/C. A mixture of epimers **21** was obtained in the same ratio as described above. Hydrolysis of cyclic carbonate **22** was cleanly achieved by treatment with 10% aqueous NaOH solution in EtOH furnishing diol

(10) It is known that commercial 10% Pd/C preparations are acidic and exhibit a marked tendency to cleave acid-sensitive alcohols protective groups such as TES or THP ethers. See, for example: Ikawa, T.; Sajiki, H.; Hirota, K. *Tetrahedron* **2004**, *60*, 6189.

(11) For example, see: (a) Thompson, H. W.; McPherson, E.; Lences, B. L. *J. Org. Chem.* **1976**, *41*, 2903. (b) MaGee, D. A.; Lee, M. L.; Decken, A. *J. Org. Chem.* **1999**, *64*, 2549.

SCHEME 9



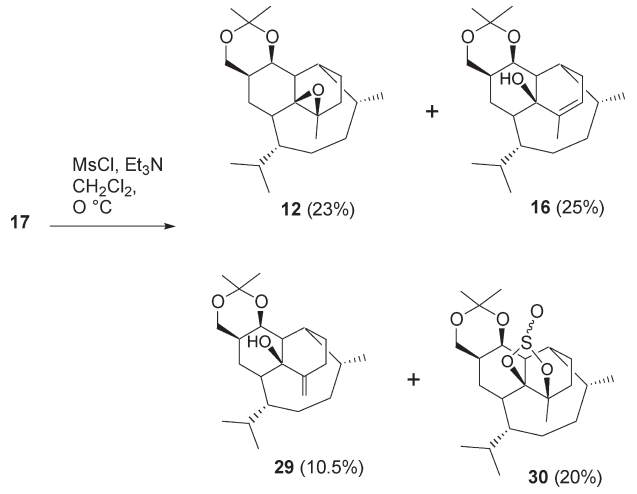
17 in almost quantitative yield. The stereochemistry of methyl group at C-9 in **17** was confirmed by X-ray crystallography.

Having diol **17** in hand, attention was directed to preparation of olefin **16** by regioselective removal of the hydroxyl group at C-8.[12] This option was based on the difference of behavior of alcohol functions at C-8 and C-8a positions. When **17** was treated with TBSOTf in the presence of 2,6-lutidine in CH_2Cl_2, only the tertiary alcohol at C-8 was protected affording TBS silyl ether **24** in high yield (Scheme 8). The hydroxyl group at C-8a proved inert to these conditions. Therefore, by subjecting diol **17** to dehydrating reagents, dehydration could occur selectively at C-8 leading to olefin **16**. To test the feasibility of this approach, the reaction was first attempted on epimer **25** (Scheme 9). Treatment of **25** with methanesulfonyl chloride and triehylamine in CH_2Cl_2 at 0 °C readily led to a separable 1:1 mixture of isomeric olefins **26** and **27** in high yield. Catalytic hydrogenation of *exo*-isomer **27** over platinum oxide in EtOH afforded tertiary alcohol **28** as the single product. The structure of **28** was determined by X-ray crystallographic analysis, which showed that the stereochemistry of both methyl groups at C-8 and C-9 are opposite to those in vinigrol. *endo*-Isomer **26** was found to be unreactive under the same conditions.

We turned then to the dehydration of major isomer **17**. Unexpectedly, treatment of diol **17** with MsCl under the conditions described above led to a mixture of five products that were separated by careful column chromatography on silica gel. The less polar compound was identified as the already known epoxide **12**. The following component was

(12) Initial attempts to prepare alcohol **14** from by reductive opening of cyclic carbonate **22** or from the corresponding cyclic sulfate were unsuccessful.

SCHEME 10



found to be an inseparable mixture of *endo*-isomer **16** and cyclic sulfite **30** according to ^{1}H and ^{13}C NMR spectra. Treatment of this mixture with $LiAlH_4$ led to a separable mixture of **16** and diol **17** that resulted from the reduction of **30**. The other products were *exo*-isomer **29** and the second isomeric cyclic sulfite (Scheme 10). To isolate pure **16**, the crude product of the reaction with MsCl-Et_3N was reduced directly, and the resulting mixture was then separated by chromatography to furnish **12** (23%), **16** (25%), **29** (10.5%), and **17** (20%). All attempts to avoid the formation of undesired products, e.g., epoxide **12** and cyclic sulfite **30**, including treatment with MsCl-DMAP or methanesulfonyl anhydride (Ms_2O), were unsuccessful. The sharp contrast in the reactivity of isomeric diols **17** and **25** toward dehydration with MsCl is not understood yet. Inspection of the X-ray structure of these isomers did not reveal any significant conformational difference except the configuration of methyl group at C-9 (see the ORTEP drawings of compounds **17** and **25** in Supporting Information). However, their ^{13}C NMR spectra exhibit striking differences: whereas **25** showed sharp signals for all carbon atoms, many of its epimer were broad or hardly observed (see Supporting Information). This anomaly, also observed for compounds 24, **16**, **31** and **32**, probably results from the presence of two conformers in a dynamic equilibrium at room temperature.

Catalytic hydrogenation of *exo*-isomer **29** over platinum oxide in EtOH for1 h afforded **31** exclusively in 75% yield. Acid-catalyzed hydrolysis of **31** led to a mixture of **32** and the dehydrated product **33** (Scheme 11). These structures were assigned on the basis of spectroscopic data, and the stereochemistry of methyl at C-8 in **32** was found to be opposite to that in vinigrol according to X-ray crystallographic analysis (Figure 2).[13] In this reaction, addition of hydrogen occurred from the same side of hydroxyl group. The approach of the catalyst surface from the other side was impeded by the severe steric hindrance due to the presence of the *ansa* belt. We turned then to catalytic hydrogenation of *endo*-isomer **16**. As for **26**, all attempts of heterogeneous or homogeneous catalytic hydrogenation were unsuccessful. Allylic alcohol **16**

(13) CCDC 747695, 747694, 747693, 747696, and 747697 (**17**, **22**, **25**, **28**, and **32**, respectively) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge crystallographic Data centre at www.ccdc.com.ac.uk/data/cif.

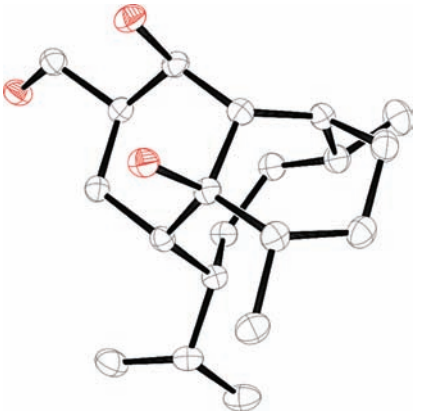
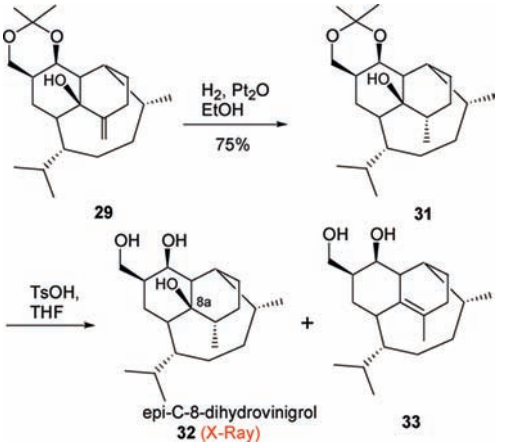


FIGURE 2. ORTEP drawing of epi-C8-dihydrovinigrol **32**.

SCHEME 11



was recovered unchanged after treatment with Pt_2O in ethanol, Rh/Al_2O_3 in ethyl acetate, or Wilkinson's catalyst in benzene under hydrogen during overnight stirring. Recourse to 10% Pd%C in EtOAc and longer reaction times resulted in hydrolysis of acetonide and dehydration of tertiary alcohols leading to chromatographically inseparable mixtures. Obviously, this lack of reactivity of **16** toward catalytic hydrogenation is the result of the steric congestion of both sides of the double bond.

Conclusions

In summary, two approaches to vinigrol starting from the advanced tricyclic core **7** have been explored using as key intermediates epoxide **12** and diol **17**. The preparation of the properly functionalized epoxide **12** has been achieved in a straightforward fashion. However, all attempts to prepare tertiary alcohol **14** by reductive opening of **12** failed. In alternative exploratory efforts to achieve the same goal, allylic alcohols **16** and **29** were prepared by regioselective dehydration of diol **17**. Although *endo*-isomer **16** was found to be reluctant to catalytic hydrogenation, the *exo* counterpart **29** led to the undesired isomer affording after hydrolysis epi-C-8-dihydrovinigrol **32**.

It appears from this study that the major problem of achieving the total synthesis of vinigrol lies not only in the construction of the tricyclic core but in the transformation of

functional groups present in this very congested structure. In particular, the intramolecular cyclization reactions were frequently observed as a result of the proximity of functionalized centers, especially between the eight-membered ring bridge and the *cis*-decalin moiety. Further efforts should be provided to achieve the challenging conquest of this intriguing class of compounds.[14]

Experimental Section

Dihydroxylation of 7. Triol 19. To a solution of ketone **7** (150 mg, 0.416 mmol) in THF (2 mL) cooled at 0 °C was added a 4.10^{-2} M solution of OsO4 in *t*-BuOH/*t*-BuOOH (5 mL, 0.2 mmol) followed by NMO (150 mg, 1.28 mmol). The solution was stirred for 2 h at room temperature and then was quenched with a saturated aqueous solution of $NaHSO_3$. The aqueous layer was extracted with EtOAc, and the combined organic fractions were dried ($MgSO_4$) and concentrated. The resulting brown solid (250 mg) was dissolved in dry ether (10 mL), treated with $LiAlH_4$ (140 mg) for 1 h at room temperature, and then quenched with 10% aqueous solution of NaOH (1 mL) at 0 °C. The mixture was stirred 30 min at room temperature, filtered through a pad of Celite and $MgSO_4$, and washed several times with EtOAc to give, after concentration, triol **19** as a white solid (146 mg), which was used in the next step without further purification. Alternatively, an analytically pure sample of **19** could be obtained by recrystallization from ethyl ether to give a white solid: mp 186−187 °C; R_f 0.55 (EtOAc/petroleum ether 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (s, 1H), 4.17−4.10 (m, 2H), 3.97 (br s, 1H), 3.76 (d, J = 2.8 Hz, 1H), 3.52 (d, J = 12 Hz, 1H), 2.59 (td, J = 15, 7.2 Hz, 1H) 2.28−2.35 (m, 2H), 2.31 (d, J = 6.4 Hz, 1H), 2.13 (d, J = 6.8 Hz, 1H), 2.00−2.12 (m, 2H), 1.80−2.10 (m, 2H), 1.60−1.80 (m, 6H), 1.42−1.44 (m, 1H), 1.47 (s, 3H), 1.42 (s, 3H), 1.21 (d, J = 7.1 Hz, 3H), 1.17 (s, 3H), 0.94 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.7 (C), 73.9 (CH), 72.8 (CH), 72.4 (2C), 63.8 (CH_2), 43.6 (CH), 43.1 (CH), 42.1 (CH), 38.0 (CH), 37.4 (CH), 34.9 (CH), 33.2 (CH_2), 32.9 (CH_2), 30.8 (CH), 30.0 (CH), 24.19 (CH_3), 23.9 (CH_3), 22.7 (CH_2), 22.4 (CH_3), 20.0 (CH_2), 19.0 (CH_3), 18.4 (CH_3); IR (cm^{-1}, CCl_4) 3628, 3441, 2958, 2872; HRMS (EI) m/e exact mass calculated for $C_{23}H_{40}O_5$ 396.2876, found 396.2858.

Cyclic Carbonate 20. To a solution of crude triol **19** (146 mg) and pyridine (0.7 mL) in dry CH_2Cl_2 (6 mL) at 0 °C was added dropwise a solution of triphosgene (550 mg, 1.85 mmol) in dry CH_2Cl_2 (2 mL). The mixture was stirred at room temperature for 24 h, and water was then added dropwise at 0 °C *very cautiously*. The aqueous layer was extracted with CH_2Cl_2, and the combined organic fractions were washed with brine, dried over $MgSO_4$, and concentrated. The crude product was purified by flash column chromatography (EtOAc/PE 1/4) affording the cyclic carbonate **20** (119 mg, 70%) as a white solid; mp 162−164 °C, R_f 0.55 (EtOAc/petroleum ether 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.59 (d, J = 7.6 Hz, 1H), 4.07(dd, J = 12, 3.2 Hz, 1H), 3.93 (d, J = 3.2 Hz, 1H), 3.51 (d, J = 12 Hz, 1H), 2.68 (br t, J = 5.6 Hz, 1H), 2.28 (td, J = 14, 5.2 Hz, 1H) 1.90−2.15 (m, 7H), 1.60−1.90 (m, 4H), 1.82 (s, 3H), 1.42−160 (m, 4H), 1.41 (s, 6H), 0.95 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1 (C), 133.1 (C), 126.5 (CH), 98.3 (C), 88.3 (C), 86.4 (C), 70.7 (CH), 63.8 (CH_2), 45.9 (CH), 43.4 (CH), 39.6 (CH), 39.3 (CH), 37.1 (CH), 31.9 (CH), 31.0 (CH_2), 29.7 (CH), 28.7 (CH), 27.9 (CH_2), 25.2 (CH_2), 23.0 (CH_2), 22.6 (CH_3), 21.7 (CH_3), 18.8 (CH_3), 17.9 (CH_3); IR (cm^{-1}, CCl_4) 2952, 2865, 1805, 1455; HRMS (EI) m/z exact mass calculated for $C_{24}H_{36}O_5$ 404.2563, found 404.2568.

Catalytic Hydrogenation of 20. Cyclic Carbonates 22 and 23. To a solution of olefin **20** (224 mg, 0.554 mmol) in EtOAc (7 mL) was added 10% Pd/C (180 mg). The flask was flushed with hydrogen and stirred under hydrogen for 24 h. The mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure to afford 227 mg of colorless residue. This crude product was dissolved in dry CH_2Cl_2 (2 mL) and treated with 2,2-dimethoxypropane (DMP) (0.75 mL) in the presence of camphorsulfonic acid (CSA) (5 mg) for 1 h. Triethylamine (few drops) was added, and the mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography (elution with 10% ethyl acetate in petroleum ether). Concentration of the appropriate fractions afforded 115 mg (51%) of the major isomer **22** and 57 mg (25%) of the minor isomer **23**

Data for 22. White solid: mp 175−177 °C; R_f 0.33 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (d, J = 5.6 Hz, 1H), 3.93 (dd, J = 11.6, 6 Hz, 1H), 3.42 (dd, J = 11.6, 5.6 Hz, 1H), 2.22−2.42 (m, 1H), 2.02−2.20 (m, 4H), 1.40−1.85 (m, 11H), 1.38 (s, 6H), 1.36 (s, 3H), 1.01 (d, J = 6 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5 (C), 99.2 (C), 89.5 (C), 85.9 (C), 70.2 (CH), 63.9 (CH_2), 48.4 (CH), 46.1 (CH), 40.6 (CH), 37.8 (CH), 37.6 (CH), 31.5 (CH_2), 30.4 (CH), 30.3 (CH), 30.2 (CH_2), 27.6 (CH_2), 27.0 (CH_3), 25.9 (CH_3), 24.3 (CH_2), 22.9 (CH_3), 22.2 (CH_3), 21.9 (CH_2), 21.0 (CH_3), 17.5 (CH_3); IR (cm^{-1}, CCl_4) 2955, 2875, 1806; HRMS (EI) m/z exact mass calculated for $C_{23}H_{35}O_5$ (M − Me) 391.2484, found 391.2477.

Data for 23. White solid: mp 192−194 °C; R_f 0.30 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (dd, J = 12, 6, 3.6 Hz, 1H), 4.06 (d, J = 3.6 Hz, 1H), 3.42 (d, J = 12, Hz, 1H), 2.37−2.47 (m, 2H), 2.00−2.20 (m, 3H), 1.42−1.80 (m, 10H), 1.44 (s, 3H), 1.43 (s, 3H), 1.42 (s, 3H), 1.02 (d, J = 6.8 Hz, 3H), 0.97 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3 (C), 98.3 (C), 89.3 (C), 86.1(C), 69.9 (CH), 63.7 (CH_2), 45.7 (CH), 45.3 (CH), 42.1 (CH), 37.6 (CH), 35.8 (CH), 34.6 (CH_2), 34.3 (CH), 32.1 (CH_2), 30.9 (CH), 29.7, 27.5 (CH_2), 26.5, 22.2 (CH_2), 22.1, 21.8, 20.9, 19.5 (CH_2), 18.7; IR (cm^{-1}, CCl_4) 2955, 2875, 1806; HRMS (EI) m/z exact mass calculated for $C_{23}H_{35}O_5$ (M − Me) 391.2484, found 391.2488. The structure of this compound was confirmed by X-ray crystallographic analysis.

Hydrolysis of Cyclic Carbonate 22. Diol 17. To a solution of the cyclic carbonate **22** (51 mg, 0.125 mmol) in ethanol (2.5 mL) was added 10% aqueous NaOH solution (1.5 mL), and the mixture was stirred at room temperature for 20 h and then concentrated under reduced pressure. The residue was partitioned between ethyl acetate and water and the aqueous phase extracted twice with ethyl acetate. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated to afford diol **17** (45 mg) as a white solid, which was used in the next step without further purification. Alternatively, an analytically pure sample of **17** could be obtained by recrystallization from petroleum ether to give a white solid: mp 110−111 °C; R_f 0.50 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.59 (br s, 1H), 4.24 (d, J = 3.6 Hz, 1H), 4.10 (dd, J = 12, 4 Hz, 1H), 4.05 (br s, 1H), 3.52 (d, J = 12 Hz, 1H), 2.46 (td, J = 13.6, 6 Hz, 1H), 2.02−2.32 (m, 5H), 1.42−1.90 (m, 11H), 1.44 (s, 3H), 1.40 (s, 3H), 1.15 (s, 3H), 1.03 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.7 (C), 72.1 (CH), 63.9 (CH_2), 34.9 (CH_2), 29.7, 29.6, 29.4, 24.4, 22.4, 18.7, all that remains of carbons were too broad to be observed; IR (cm^{-1}, CCl_4) 3424, 2955, 2872; HRMS (EI) m/z exact mass calculated for $C_{23}H_{40}O_4$ 380.2927, found 380.2909. The structure of this compound was confirmed by X-ray crystallographic analysis.

(14) While the manuscript was under revision, Baran and coworkers published the first total synthesis of vinigrol. Maimone, T. J.; Shi, J.; Ashida, S.; Baran, P. S. *J. Am. Chem. Soc.* ASAP October 30 2009, DOI: 10 1021/ja908194b.

TBS Silyl Ether 24. To the solution of the aforementioned diol **17** in dry DCM (1.2 mL) cooled at 0 °C and stirred under nitrogen was added 2,6-lutidine (70 μL, 0.60 mmol) followed by TBSOTf (45 μL, 0.19 mmol). The cooling bath was removed, and the solution was stirred for 1 h at room temperature. Water was added, and the product was extracted with DCM. The organic extracts were combined, washed with brine, dried ($MgSO_4$), and concentrated, and the resulting residue was purified by column chromatography (2.5% EtOAc in PE) to afford the TBS ether **24** (50 mg, 80% from **22**) as a white foam: R_f 0.25 (2.5% EtOAc in PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (d, J = 3.6 Hz, 1H), 3.86 (br s, 1H), 3.50 (dd, J = 11.6, 5.2 Hz, 1H), 1.88−2.40 (m, 6H), 1.40−1.85 (m, 6H), 1.39 (s, 3H), 1.33 (s, 3H), 1.21 (s, 3H), 1.01 (d, J = 6.4 Hz, 3H), 0.80−0.95 (M, 15H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.8 (C), 78.3(C), 71.5 (CH), 64.3 (CH_2), 41.9 (CH), 37.7 (CH_2), 26.20 (3 CH_3), 29.7, 23.8, 22.4, 18.8, −1.81, −2.04, all that remains of carbons were too broad to be observed; IR (cm^{-1}, CCl_4) 3456, 2931, 2872; HRMS (EI) m/z exact mass calculated for $C_{29}H_{54}O_4Si$ 494.379, found 494.3782.

Hydrolysis of Cyclic Carbonate 23. Diol 25. Hydrolysis of cyclic carbonate **23** (68 mg, 0.167 mmol) was carried out in the same manner as for **22** to afford diol **25** (59 mg) as a white solid, which was used in the next step without further purification. Alternatively, an analytically pure sample of **25** could be obtained by recrystallization from petroleum ether to give a white solid: mp112−113 °C; R_f 0.40 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.51 (s, 1H), 4.16 (m, 2H), 3.74 (s, 1H), 3.54 (d, J = 12 Hz, 1H), 2.25 (td, J = 14, 7.2 Hz, 1H), 2.31 (d, J = 5.6 Hz, 1H), 2.22 (d, J = 6.8 Hz, 1H), 2.1 (m, 1H), 1.42−1.95 (m, 13H), 1.47 (s, 3H), 1.42 (s, 3H), 1.18 (s, 3H), 0.99−0.92 (3d, J = 6.8 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.7 (C), 72.8 (CH), 72.1 (2C), 63.9 (CH_2), 44.6 (CH), 43.3 (CH), 41.9 (CH), 41.7 (CH), 36.0 (CH), 34.7 (CH_2), 34.5 (CH), 33.6 (CH_2), 31.2 (CH), 30.0 (CH), 27.8 (CH_3), 27.0 (CH_2), 23.7 (CH_3), 22.2 (CH_3), 21.5 (CH_2), 21.2 (CH_3), 18.8 (CH_2), 18.7 (CH_3); IR (cm^{-1}, CCl_4) 3442; HRMS (EI) m/z exact mass calculated for $C_{23}H_{40}O_4$ 380.2926, found 380.2958. The structure of this compound was established by X-ray crystallographic analysis.

Alkenes 26 and 27. To a solution of crude diol **25** (10 mg, 0.026 mmol) and Et_3N (60 μL, 0.42 mmol) in 0.5 mL of CH_2Cl_2 at 0 °C was added MsCl (30 μL, 0.39 mmol). The resulting mixture was stirred for 1 h at 0 °C, quenched with 0.5 mL of saturated $NaHCO_3$, and extracted with ether. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and evaporated to yield a crude mixture of alkenes and . The crude residue was purified by flash chromatography (elution with 5% ethyl acetate in petroleum ether). Concentration of the appropriate fractions afforded 4.2 mg of the *endo*-isomer **26** and 4 mg of the *exo*-isomer **27**.

***endo*-Isomer 26.** R_f 0.50 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (br s, 1H), 4.93 (s, 1H), 4.16 (m, 2H), 3.55 (d, J = 11.6 Hz, 1H), 2.54 (td, J = 14, 7.2 Hz, 1H), 2.37 (d, J = 7.2 Hz, 1H), 2.25 (m, 1H), 2.17 (d, J = 6 Hz, 1H), 2.1−1.9 (m, 2H), 1.72 (d, J = 1.2 Hz, 3H), 1.80−1.55 (m, 3H), 1.47 (s, 3H), 1.41 (s, 3H), 1.50−1.40 (m, 3H), 1.25−1.15 (m, 3H), 1.00−0.91 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4 (C), 123.9 (CH), 98.7 (C), 73.92 (C), 73.2 (CH), 64.3 (CH_2), 47.9 (CH), 47.4 (CH), 41.9 (CH), 41.1 (CH), 35.2 (CH), 35.1 (CH), 32.4 (CH_2), 32.2 (CH), 30.1 (CH), 28.7 (CH_2), 26.7 (CH_3), 24.8 (CH_2), 21.9 (CH_3), 21.7 (CH_3), 19.4 (CH_2), 18.5 (CH_3), 17.0 (CH_3); IR (cm^{-1}, CCl_4) 3500; HRMS (EI) m/z exact mass calculated for $C_{23}H_{38}O_3$ 362.2821, found 362.2827.

***exo*-Isomer 27.** R_f 0.45 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.29 (s, 1H), 5.22 (br s, 1H), 4.97(br s, 1H), 4.17 (m, 2H), 3.53 (d, J = 11.6 Hz, 1H), 2.56 (td, J = 14, 6.8 Hz, 1H), 2.48 (t, J = 6.4 Hz, 1H), 2.17 (d, J = 6.8 Hz, 1H), 2.10−1.45 (m, 8H), 1.47 (s, 3H), 1.41 (s, 3H), 1.48−1.40 (m, 6H), 0.99 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0 (C), 110.4 (CH_2), 98.7 (C), 75.1 (C), 72.1 (CH), 64.1 (CH_2), 47.6 (CH), 45.7 (CH), 44.5 (CH), 41.4 (CH), 36.7 (CH), 34.3 (CH_2), 34.2 (CH), 32.7 (CH_2), 30.6 (CH), 30.0 (CH_3), 27.8 (CH_2), 26.6 (CH_3), 23.1 (CH_2), 21.6 (CH_2), 21.2 (CH_3), 20.5 (CH_3), 18.5 (CH_3); IR (cm^{-1}, CCl_4) 3485; CI MS: NH_3 m/z 363 ($M^{+\bullet}$ + 1), 380 (M + 18); HRMS (EI) m/z exact mass calculated for $C_{23}H_{38}O_3$ 362.2821, found 362.2832.

Catalytic Hydrogenation of 27. Alcohol 28. To a solution of olefin **27** (14 mg, 0.038 mmol) in Et0H (0.75 mL) was added 10% PtO_2 (10 mg). The flask was flushed with hydrogen and stirred under hydrogen for 1 h. The mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure to afford colorless residue. Purification of the crude by flash chromatography (elution with 5% ethyl acetate in petroleum ether) led to 10 mg (71%) of **28** as a white solid: mp123−125 °C. R_f 0.5 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.30 (s, 1H), 4.14 (m, 2H), 3.53 (d, J = 12 Hz, 1H), 2.45 (td, J = 14, 7.2 Hz, 1H), 2.30 (t, J = 6.8 Hz, 1H), 2.20−1.40 (m, 16H), 1.46 (s, 3H), 1.40 (s, 3H), 1.06 (d, J = 6.4 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.6 (C), 74.3 (C), 73.2 (CH), 64.1 (CH_2), 50.0 (CH), 44.6 (CH), 43.3 (CH), 42.9 (CH), 41.6 (CH), 36.3 (CH), 34.5 (CH), 33.8 (CH_2), 31.5 (CH_2), 31.4 (CH), 30.1 (CH_3), 27.8 (CH_2), 27.0 (CH_3), 24.6 (CH_2), 22.3 (CH_3), 21.5 (CH_2), 21.0 (CH_3), 18.4 (CH_3), 14.2 (CH_3); IR (cm^{-1}, CCl_4) 3495; HRMS (EI) m/z exact mass calculated for $C_{23}H_{40}O_3$ 364.2977, found 364.2975. The structure of this compound was established by X-ray crystallographic analysis.

Alkenes 16 and 29. To a solution of crude diol **17** (90 mg, 0.236 mmol) and Et_3N (0.6 mL, 2.85 mmol) in 2.5 mL of CH_2Cl_2 cooled at 0 °C was added Ms_2O (500 mg, 2.87 mmol) in 1 mL of CH_2Cl_2. The resulting mixture was stirred for 1 h at 0 °C, quenched with 1 mL of saturated $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and evaporated to yield a mixture of products as a pale residue. The crude product was dissolved in dry 2.5 mL of ether, treated at 0 °C with $LiAlH_4$ (40 mg) for 1 h, and quenched with 10% aqueous solution of NaOH, and the resulting precipitate was filtered through Celite. The filter cake was washed with ether, and the filtrate was dried over $MgSO_4$. Evaporation of the solvent gave a mixture that was separated by flash chromatography (elution with 10% ethyl acetate in petroleum ether). Concentration of the appropriate fractions afforded epoxide **12** (20 mg, 23%), *endo*-isomer **16** (21 mg, 25%), *exo*-isomer **29** (9 mg, 10.5%), and the starting diol **17** (18 mg, 20%).

***endo*-Isomer 16.** R_f 0.50 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.55 (d, J = 5.6 Hz, 1H), 4.87 (br s, 1H), 4.22 (d, J = 3.2 Hz, 1H), 4.14 (dd, J = 11.6, 3.2 Hz, 1H), 3.56 (d, J = 12 Hz, 1H), 2.52 (td, J = 14, 6.4 Hz, 1H), 2.40−1.80 (m, 5H), 1.72 (d, J = 1.2 Hz, 3H), 1.75−1.25 (m, 12H), 1.46 (s, 3H), 1.39 (s, 3H), 0.92 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.8 (CH), 98.6 (C), 64.1 (CH_2), 37.0, 30.3, 29.9, 22.1, 21.5, 18.5, all that remains of carbons were too broad to be observed; IR (cm^{-1}, CCl_4) 3495; HRMS (EI) m/z exact mass calculated for $C_{23}H_{38}O_3$ 362.2821, found 362.2802.

***exo*-Isomer 29.** R_f 0.40 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.25 (br s, 1H), 5.02 (br s, 1H), 4.97(s, 1H), 4.23 (d, J = 3.6 Hz, 1H), 4.12 (dd, J = 12, 4 Hz, 1H), 3.52 (d, J = 12 Hz, 1H), 2.65 −2.40 (m, 3H), 2.20 −2.00 (m, 4H), 1.80−1.40 (m, 10H), 1.45 (s, 3H), 1.39 (s, 3H), 1.01 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7 (C), 111.7 (CH_2), 98.7 (C), 75.3 (C), 72.9 (CH), 64.1 (CH_2), 51.6 (CH), 45.5 (CH), 45.1 (CH), 36.9 (CH), 32.8 (CH_2), 32.6 (CH_2), 31.1 (CH_2), 30.3 (CH), 29.7 (CH), 29.5 (CH), 29.3 (CH_3), 25.9 (CH_2), 25.0 (CH_3), 22.5 (CH_2), 20.5 ($2CH_3$), 18.8 (CH_3); IR (cm^{-1}, CCl_4) 3485; CI MS NH_3 m/z 363

($M^{+\bullet}$ + 1), 380 (M + 18); HRMS (EI) *m*/*z* exact mass calculated for $C_{23}H_{38}O_3$ 362.2821, found 362.2832.

Alcohol 31. To a solution of olefin **29** (8 mg, 0.022 mmol) in Et0H (0.5 mL) was added 10% PtO_2 (10 mg). The flask was flushed with hydrogen and stirred under hydrogen for 1 h. The mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure to afford colorless residue. Purification of the crude by flash chromatography (elution with 5% ethyl acetate in petroleum ether) led to 6 mg (75%) of **31** as a white solid: mp120−122 °C (PE); R_f 0.45 (EtOAc/PE 1/9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (br s, 1H), 4.22 (d, J = 3.6 Hz, 1H), 4.09 (dd, J = 12, 4 Hz, 1H), 3.51 (d, J = 12 Hz, 1H), 2.45−1.40 (m, 19H), 1.45 (s, 3H), 1.40 (s, 3H), 1.04 (d, J = 6.4 Hz, 3H), 1.03 (d, J = 6.4 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.7 (C), 74.9 (C), 73.0 (CH), 64.1 (CH_2), 50.0 (CH), 45.2, 31.2, 29.8, 27.0 (CH_3), 22.6, 22.5 (CH_2), 19.0, 14.9 (CH_3), all that remains of carbons were too broad to be observed; IR (cm^{-1}, CCl_4) 3495; IR (cm^{-1}, CCl_4) 3490; CI MS NH_3 *m*/*z* 271, 289, 364 ($M^{+\bullet}$.), 365 ($M^{+\bullet}$ + 1); HRMS (EI) *m*/*z* exact mass calculated for $C_{23}H_{40}O_3$ 364.2978, found 364.2989.

Hydrolysis of Acetonide 31. To a stirred solution of acetonide **31** (5 mg, 13.7 μmol) in aqueous THF (0.5 mL) were added a few crystals of TsOH acid. The mixture was stirred for 7 h, and then three drops of Et_3N were added. Evaporation of the solvent followed by purification of the crude by flash chromatography (elution with 20% ethyl acetate in petroleum ether) led to triol **32** (2 mg) and diol **33** (2 mg).

Triol 32. White solid: mp 207−210 °C; R_f 0.2 (EtOAc/PE 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (br s, 1H), 3.83 (br d, J = 12 Hz, 1H), 3.72 (m, 1H), 2.80 (br s, 1H), 2.45−1.40 (m, 2 H), 2.12 (d, J = 5.2 Hz, 1H), 2.10−1.95 (m, 2H), 1.90−1.40 (m, 15H), 1.05 (d, J = 7.2 Hz, 3H), 1.02 (d, J = 6.4 Hz, 3H), 0.94 (d, J = 6.4 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 78.4 (C), 74.7 (CH), 66.8 (CH_2), 45.9, 36.0, 31.4, 22.4, 14.3, all that remains of carbons were too broad to be observed; IR (cm^{-1}, CCl_4) 3676, 3622, 3361 (br); IR (cm^{-1}, CCl_4) 3606; HRMS (EI) *m*/*z* exact mass calculated for $C_{20}H_{36}O_3$ 324.2665, found 324.2651. The structure of this compound was confirmed by X-ray crystallographic analysis.

Diol 33. R_f 0.4 (EtOAc/PE 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.48 (dd, J = 10.8, 3 Hz, 1H), 3.83 (t, J = 10.4 Hz, 1H), 3.52 (dd, J = 10.8, 5.2 Hz, 1H), 3.03 (m, 1H), 2.50 (br s, 1H), 2.45−2.30 (m, 2 H), 2.25−1.85 (m, 4H), 1.72 (d, J = 0.8 Hz, 3H), 1.70−1.20 (m, 11H), 1.19 (d, J = 7.6 Hz, 3H), 0.91 (T, J = 6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.4 (C), 128.4 (C), 73.3 (CH), 64.6 (CH_2), 54.4 (CH), 45.4 (CH), 41.1 (CH), 41.0 (CH), 38.4 (CH), 31.1 (CH), 30.6 (CH_2), 30.5 (CH), 30.2 (CH_2), 29.7 (CH_2), 24.8 (CH_2), 21.7 (CH_3), 21.3 (CH_3), 21.2 (CH_3), 20.2 (CH_2), 18.5 (CH_3); IR (cm^{-1}, CCl_4) 3621, 3539, 3363 (br) ; HRMS (EI) *m*/*z* exact mass calculated for $C_{20}H_{32}O$ (M − H_2O) 288.2453, found 288.2458.

Supporting Information Available: Experimental procedures for compounds **8**−**13**, **15**, **18**; ^{1}H and ^{13}C NMR spectra for all new compounds; and X-ray crystallographic data of compounds **17**, **23**, **25**, **28**, and **32** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.