Total Synthesis of (±)-Africanol and (±)-Isoafricanol

Weiming Fan and James B. White*

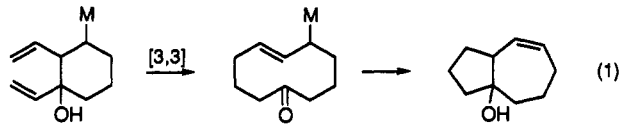
Department of Chemistry, Box 19065, The University of Texas at Arlington, Arlington, Texas, 76019

Received March 1, 1993

A six-step synthesis of the sesquiterpenes africanol and isoafricanol from 3,5,5-trimethylcyclohex-2-en-1-one is reported. The anionic oxy-Cope rearrangement is used to prepare substituted 5-cyclodecenones functionalized with an allylstannane moiety, which, upon cyclization with the ketone, lead to hydroazulene derivatives. The stereochemistry in the transannular cyclization can be controlled through the choice of reaction conditions both with respect to the ring fusion itself and with respect to a preexisting chiral center. Cyclopropanation of the alkene that is generated following cyclization completes the synthesis of both compounds.

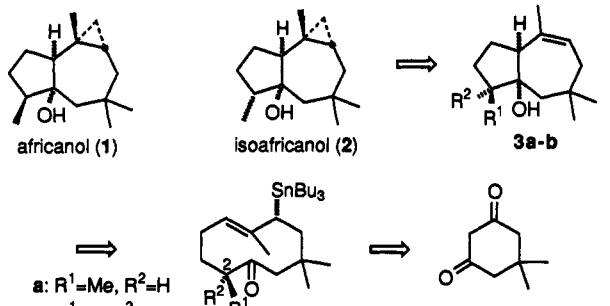
Introduction

Our original approach to the synthesis of hydroazulenes involved a two-step sequence in which the key step was a transannular cyclization of an allylsilane to a ketone within a 5-cyclodecenone (eq 1, M = $SiMe_3$).[1a] In effect,

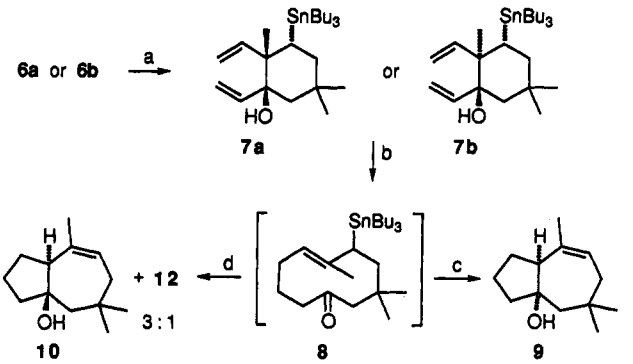


(1)

the chirality within the allylsilane moiety is exchanged in the cyclization step for the two chiral centers of the bridgeheads of the hydroazulene. Our subsequent finding[1b] that the choice of reaction conditions can be used to control the stereochemistry in the cyclization of the corresponding allylstannane (M = $SnBu_3$) encouraged us to utilize this methodology in stereochemically controlled syntheses of the sesquiterpenes africanol (**1**)[2a] and isoafricanol (**2**).[2b] Both of these compounds[3] are structurally characterized as cis-fused hydroazulenols, differing only in their relative stereochemistry within the five-membered ring. It was anticipated from model studies[4] that africanol and isoafricanol could be derived from 5-cyclodecenones **4a,b**. In the proposed cyclizations of **4a,b** there is a more strenuous test to be met with respect to control over relative stereochemistry than is the case in eq 1. The additional chiral center at C2 of the cyclodecenone requires not only discrimination between cis and trans ring fusions, but also between two different cis ring fusion diastereomers. We report herein the synthesis of racemic africanol and isoafricanol, as well as some additional work related to these transannular cyclizations.



Scheme I[a]



[a] Reagents: (a) CH_2=CHMgBr, $CeCl_3$, THF, −78 °C; (b) KH, ether, rt, 5 h; (c) *n*-Bu_4NF, THF, rt, 5 h; (d) SiO_2.

Results and Discussion

Auxiliary Study. In the course of synthesizing africanol and isoafricanol, several other reactions were carried out that are of general interest with respect to our overall goals for this project. As an alternative route to cyclodecenones **4a,b**, a mixture of vinylmagnesium bromide and $CeCl_3$ was added to cyclohexanones **6a,b**, leading to divinylcyclohexanols **7a,b** (Scheme I). In principle, 5-cyclodecenones **4a,b** could have been derived from **7a,b** through methylation of the intermediate enolates from anionic oxy-Cope rearrangement. In practice, the alkylation proved unworkable, a result not wholly unexpected based on anomalies we had observed in alkylations of related enolates.[5] However, cyclodecenone **8**, which lacks the stereocenter at C2, was prepared from either **7a** or **7b** upon standard workup, and its cyclization was examined. When the crude ketone from the oxy-Cope rearrangement was treated with *n*-Bu_4NF it gave the expected[1b] cis-fused hydroazulenol **9**. Lacking the methyl group at C2 of the cyclodecenone, **8** was significantly more reactive than cyclodecenones **4a,b** (vide infra), and attempts at purifying

(1) (a) Jisheng, L.; Gallardo, T.; White, J. B. *J. Org. Chem.* **1990**, *55*, 5426–5428. (b) Fan, W.; White, J. B. *Tetrahedron Lett.* **1993**, *34*, 957–960.

(2) (a) Tursch, B.; Braekman, J. C.; Daloze, D.; Fritz, P.; Kelecom, A.; Karlsson, R.; Losman, D. *Tetrahedron Lett.* **1974**, 747–750. (b) Abraham, W.-R.; Ernst, L.; Witte, L.; Hanssen, H.-P.; Sprecher, E. *Tetrahedron* **1986**, *42*, 4475–4480.

(3) For previous synthetic approaches to these compounds, see: (a) Shirahama, H.; Hayano, K.; Kanemoto, Y.; Misumi, S.; Ohtsuka, T.; Hashiba, N.; Furusaki, A.; Murata, S.; Noyori, R.; Matsumoto, T. *Tetrahedron Lett.* **1980**, *21*, 4835–4838. (b) Paquette, L. A.; Ham, W. H. *Tetrahedron Lett.* **1986**, *27*, 2341–2344. (c) Paquette, L. A.; Ham, W. H. *J. Am. Chem. Soc.* **1987**, *109*, 3025–3036. (d) Sugimura, T.; Futagawa, T.; Tai, A. *Chem. Lett.* **1990**, 2295–2298.

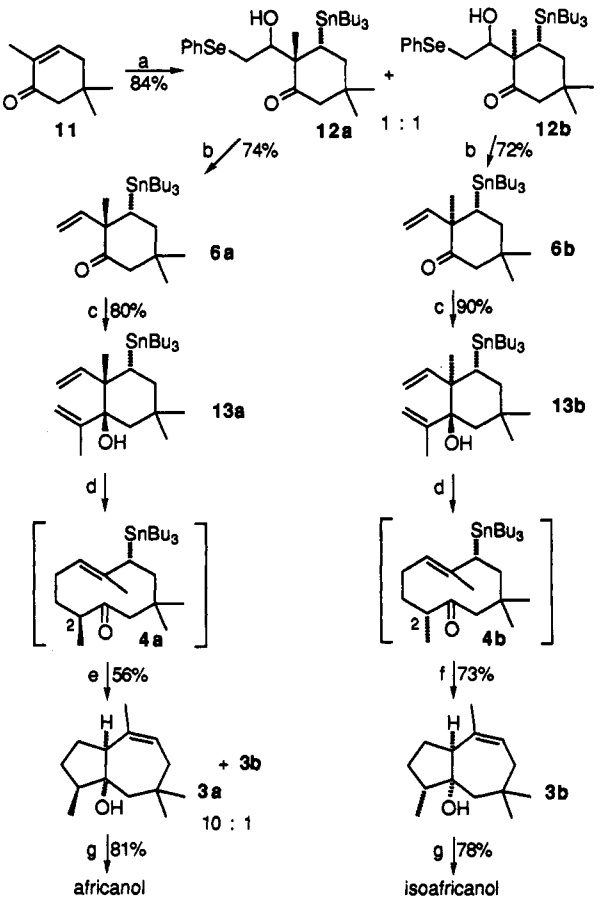
(4) Unpublished results from our group (Yongliang Chu).

0022-3263/93/1958-3557$04.00/0

it on silica gel led to its cyclization to give predominantly the trans-fused hydroazulenol **10**.

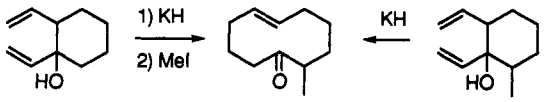
Synthesis of Africanol (1) and Isoafricanol (2). Conjugate addition of Bu_3SnLi[6] to 2,5,5-trimethylcyclohex-2-enone (**11**), which is derived in three steps from commercially available dimedone (**5**),[7] followed by in situ trapping of the intermediate enolate with the vinyl cation equivalent (phenylseleno)acetaldehyde[8] gave a separable 1:1 mixture of the aldol products **12a** and **12b** (Scheme II). It is at this point that the synthesis of africanol and isoafricanol diverged, as **12a** was carried on to 5-cyclodecenone **4a** and **12b** on to 5-cyclodecenone **4b**. Elimination to complete the introduction of the first vinyl substituent led to the cyclohexanones **6a** and **6b**. The relative stereochemistry of these compounds was assigned from comparison of the chemical shift of their C2 methyl groups in C_6D_6 and $CDCl_3$.[9] Addition of Grignard reagents to the sterically hindered ketones were sluggish, but addition of the reagent prepared at −78 °C from isopropenylmagnesium bromide and anhydrous $CeCl_3$[10] to both **6a** and **6b** each led to a single divinylcyclohexanol with the assumed stereochemistry drawn for **13a** and **13b**, respectively, from equatorial addition to the ketone.[11] These assignments were also consistent with the transformation of these compounds into africanol (**1**) and isoafricanol (**2**). Anionic oxy-Cope rearrangement[12] of **13a** and **13b** was carried out in ether and gave the 5-cyclodecenones **4a** and **4b**,[13] which were unstable and used without further purification. The optimal conditions for inducing cyclization of **4a** to give the desired cis,trans isomer **3a** were use of $Na/C_{10}H_8$ in THF, which led to a 10:1 ratio (56% from **13a**) of **3a** and the other cis ring fusion isomer, hydroazulenol **3b**.[14] Treatment of **4b** with fluoride (*n*-Bu_4NF, THF, 25 °C, 73% from **9b**) gave hydroazulenol **3b** with the cis,cis geometry characteristic of isoafricanol (**2**). Hydroazulenols **3a,b** were cleanly cyclopropanated[15] to give africanol (**1**) and isoafricanol (**2**), respectively, with addition occurring from the less hindered convex face that also bears a hydroxy group. The physical properties and spectroscopic data of synthetic **1** and **2** matched the published data.[2,3c] The overall yield for this six-flask sequence from 2,5,5-trimethylcyclohex-2-enone is approximately 11% for africanol and 15% for isoafricanol. This methodology represents a new approach to these molecules and illustrates the advantage that transannular cyclizations have for controlling the stereochemistry of the ring fusion of hydroazulenes.

Scheme II[a]



[a] Reagents: (a) *n*-Bu_3SnLi, THF, −78 °C, 30 min; $PhSeCH_2CHO$; (b) MsCl, Et_3N, CH_2Cl_2, rt, 5 h; (c) $CH_2{=}C(CH_3)MgBr$, $CeCl_3$, THF, −78 °C, 1 h; (d) KH, ether, rt, 2–3 h; (e) $Na/C_{10}H_8$, THF, rt, 15 min; (f) *n*-Bu_4NF, THF, rt, 3 h; (g) CH_2I_2, Et_2Zn, $ClCH_2CH_2Cl$, 0 °C, 10–30 min.

(5) For example, quenching of the intermediate enolate from anionic oxy-Cope rearrangement of 1,2-divinylcyclohexanol with MeI gave 10-methyl- and not the expected 2-methyl-5-cyclodecenone (unpublished results of Yongliang Chu).



This result requires isomerization of the first formed enolate, which could take place either by direct isomerization or through a series of proton transfers during the alkylation step. This preference for enolization between C1–C10 over C1–C2 is a consequence of lessened angle strain due to the planarity of the C2–C1–C10–C9 unit in (*E*)-5-cyclodecenones. For an example of the same regiochemistry from direct deprotonation of an (*E*)-5-cyclodecenone, see: (a) Schreiber, S. L.; Santini, C. *J. Am. Chem. Soc.* **1984**, *106*, 4038–4039. (b) Kitahara, T.; Mori, M.; Mori, K. *Tetrahedron* **1987**, *43*, 2689–2699.

(6) (a) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836–4838. (b) Sato, T.; Watanabe, M.; Watanabe, T.; Onoda, Y.; Murayama, E. *J. Org. Chem.* **1988**, *53*, 1894–1899.

(7) Ellis, J. E.; Dutcher, J. S.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 2670–2676.

(8) (a) Kowalski, C. J.; Dung, J.-S. *J. Am. Chem. Soc.* **1980**, *102*, 7950–7951. (b) Clive, D. L. J.; Russell, C. G.; Suri, S. C. *J. Org. Chem.* **1982**, *47*, 1632–1641.

(9) Based on the aromatic solvent-induced shifts (ASIS) method (Fétizon, M.; Goré, J.; Laszlo, P.; Waegell, B. *J. Org. Chem.* **1966**, *31*, 4047–4049), the compound exhibiting a downfield shift (for **6a**: $\delta_{C_6D_6} - \delta_{CDCl_3} = +0.23$) should be the compound with the equatorial methyl group, and the compound exhibiting an upfield shift (for **6b**: $\delta_{C_6D_6} - \delta_{CDCl_3} = -0.17$) should be the compound with the axial orientation for this methyl group. For a similar use of this method, see: Zhao, R.-B.; Wu, Y.-L. *Youji Huaxue* **1989**, *9*, 547–552.

(10) (a) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392–4398. (b) Imamoto, T. *Pure Appl. Chem.* **1990**, *62*, 747–752. (c) Imamoto, T.; Hatajima, T.; Ogata, K. *Tetrahedron Lett.* **1991**, *32*, 2787–2790.

(11) For a leading example, see: Marvell, E. N.; Whalley, W. *Tetrahedron Lett.* **1970**, 509–512.

(12) For a recent review, see: Paquette, L. A. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 609–626.

(13) The stereochemical assignments of 5-cyclodecenones **4a,b** are tentative but have strong mechanistic support. The anionic oxy-Cope rearrangement of a 1,2-divinylcyclohexanol with either a trans relationship between the vinyl substituents (e.g., **13b**) or a cis relationship (e.g., **13a**) as well established to lead to the (*E*)-stereoisomer in the product (for examples see ref 8b). The stereochemistry at C2 of **4a,b** has been assigned on the assumption of kinetic protonation of the intermediate enolates.

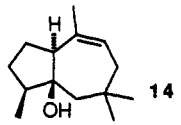
(14) The relative stereomisty at the ring fusion was determined through a comparison of the ^1H NMR spectra in pyridine-d_5 and $CDCl_3$ (Demarco, P. V.; Farkas, E.; Doddrell, D.; Mylari, B. L.; Wenkert, E. *J. Am. Chem. Soc.* **1968**, *90*, 5480–5486), which showed a slight upfield shift in pyridine-d_5 shift for the bridgehead hydrogen in the trans ring fusion and a significant downfield shift (approximately 0.35 ppm) for the cis ring fusion. The relative stereochemistry between the methyl-bearing chiral center in the cyclopentane ring and the adjacent hydroxy-bearing bridgehead carbon (either cis or trans) was similarly determined from the differences in chemical shift of the methyl group in pyridine-d_5 versus $CDCl_3$. See ref 1 for examples of this technique in the hydroazulene ring system.

(15) Denmark, S. E.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974–6981.

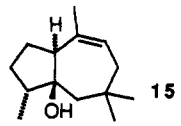
Table I. Diastereoselectivity in the Cyclizations of Cyclodecenones 4a,b

		products (% isolated yields)			
substrate	condns	3a (cis,trans)	3b (cis,cis)	14 (trans,cis)	15 (trans,trans)
4a (trans)	$Na/C_{10}H_8$	51	5		
4a (trans)	$SnCl_4$	53		10	
4a (trans)	n-Bu_4NF	12		52	
4a (trans)	SmI_2	12		62	
4a (trans)	CF_3CO_2H			65	
4b (cis)	$Na/C_{10}H_8$		70		
4b (cis)	$SnCl_4$		43		14
4b (cis)	n-Bu_4NF		73		
4b (cis)	SmI_2		64		
4b (cis)	CF_3CO_2H		38		33

With respect to the transannular cyclization of cyclodecenones **4a,b**, a variety of reaction conditions were examined, and these are summarized in Table I, which includes those already presented in the synthesis of africanol and isoafricanol. As had been observed in the cyclization of 7-(tri-*n*-butylstannyl)-5-cyclodecenone,[1b] the choice of reaction conditions greatly affects the stereochemical outcome of the transannular ring closure, and even though a total of four different diastereomers are possible products in the cyclization of either **4a** or **4b**, good diastereoselectivity was observed. Certain reagents appear to be very selective for obtaining a cis ring fusion regardless of the stereochemistry in the cyclodecenone, with $Na/C_{10}H_8$ being the most selective of all. There is also a notable substrate dependency in the diastereoselectivity. Reminiscent of the diastereoselectivity of the parent ring system,[1b] *cis*-cyclodecenone **4b** exhibited a preference for the cis ring fusion isomer **3b**, with the protic acid CF_3CO_2H showed the lowest selectivity. The surprise in this study was the propensity of cyclodecenone **4a** to undergo cyclization to give hydroazulenol **14** with the trans ring fusion. Particularly noteworthy were its reaction with fluoride, which is the first example we have found of a fluoride-mediated cyclization leading to a trans ring fusion as the major product, and with SmI_2, which also lead to a trans ring fusion and is in marked contrast to that of the other one-electron reducing agent in this study, $Na/C_{10}H_8$. It should be noted that no evidence has been found under any set of reaction conditions for 1,3-metallotropic rearrangement of the allylstannane moiety prior to cyclization. Furthermore, **3a,b** and **14** were recovered unchanged upon exposure to n-Bu_4NF/THF/rt, and likewise **3a,b** to treatment with $Na/C_{10}H_8$/THF/rt, indicating that the products from these cyclizations are kinetic in nature.



14



15

Conclusion

In summary, we have demonstrated that the transannular cyclization of allylstannanes within 5-cyclodecenones is an effective methodology for synthesizing hydroazulenes with control of the stereochemistry of the ring fusion. It should be noted that three of the four possible diastereomers from the cyclization step (i.e., **3a,b** and **14**) can be made with good to exclusive selectivity. There are two parameters that play interrelated roles in determining the stereochemical outcome of these cyclizations. One is the choice of reaction conditions, which, by affecting the mechanism of the cyclization, can in effect select certain conformation(s) over others. The other parameter is the substituents within the 10-membered ring and their stereochemical relationships, as these through steric and other effects can disfavor a particular conformation that would otherwise be favored by the choice of reaction conditions. To these ends, model studies are in progress to correlate the diastereoselectivity in these cyclizations to the choice of reaction conditions and to the stereochemistry within the ring.

Experimental Section

General. Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without further purification. Ether and tetrahydrofuran (THF) were distilled under nitrogen from sodium/benzophenone. Dichloromethane was distilled from P_2O_5. Diisopropylamine, hexamethyldisilazane, and triethylamine were distilled from CaH_2 and stored over KOH. Reactions involving organometallic reagents were carried out under argon in oven-dried glassware. Reactions were monitored by thin-layer chromatography using Whatman precoated glass plates of 250-μm thickness silica gel with a fluorescent indicator. Rt is used as an abbreviation for room temperature (16–26 °C). Flash chromatography was carried out using silica gel (35–70 μm, 60-Å pore) purchased from Scientific Adsorbents, Inc. HPLC was performed on a Waters Model 590 pump (flow rate of 20 mL/min) equipped with a Waters differential refractometer R403 using a Rainan Dynamax Macro-HPLC silica gel column (21.4-mm i.d. × 25-cm length). IR spectra were recorded on a Perkin-Elmer 1310 IR spectrophotometer. ^1H NMR spectra were recorded as solutions on a Nicolet NT-200 WB. Chemical shifts are expressed in parts per million (δ units) relative to internal tetramethylsilane (δ 0.0) or $CHCl_3$ (δ 7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad), coupling constant(s), and integration. ^{13}C NMR spectra were determined as solutions in $CDCl_3$ on a Nicolet NT-200 WB and the chemical shifts are reported in parts per million (δ units) relative to the center peak of $CDCl_3$ (δ 77.0). Low-resolution mass spectra were obtained on a GC-Finnegan TSQ 70 quadrapole mass spectrometer. Combustion analyses were obtained using a Perkin-Elmer 2400 C,H,N analyzer.

(2*S,3*R**)- and (2*R**,3*R**)-3-(Tri-*n*-butylstannyl)-2,5,5-trimethyl-2-[2-(phenylseleno)-1-hydroxyethyl]cyclohexanone (12a and 12b).** To a solution of diisopropylamine (5.88 mL, 42 mmol) in THF (100 mL) at 0 °C was added *n*-BuLi (36.51 mL, 42 mmol, 1.15 M in hexane). After 10 min, Bu_3SnH (11.31 mL, 42 mmol) was added neat. After 10 min, the mixture was cooled to −78 °C and 2,5,5-trimethylcyclohexenone[7] (4.80 g, 35 mmol) in THF (5 mL) was added slowly in one portion. After 30 min, (phenylseleno)acetaldehyde[8] (8.40 g, 42 mmol) in THF (5 mL) was added in a single portion. The mixture was stirred for 5 min, quenched with saturated NH_4Cl (60 mL), and diluted with Et_2O (100 mL). The organic layer was washed with saturated NaCl (2 × 60 mL) and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (20:1 hexanes/ethyl acetate) to give a mixture of **12a** and **12b** (18.49 g, 30 mmol, 84%). This mixture was separated by HPLC to give pure fractions of **12a** and **12b** (1:1) as colorless oils. For **12a**: IR (film) 3470, 3060, 2900, 2860, 1680, 1650, 1575, 1450, 1375, 1280, 1075, 980, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.18–7.50 (m, 5 H), 3.76–3.81 (m, 1 H), 2.47–2.63 (m, 4 H), 2.09 (s, 1 H), 0.71–1.74 (m, 39 H); ^{13}C NMR ($CDCl_3$) δ 214.0, 135.1, 129.4, 128.4, 127.5, 67.3, 56.1, 52.7, 40.7, 39.1, 33.9, 33.4, 31.8, 29.3, 27.6, 25.0, 16.2, 13.7, 11.3. Anal. Calcd for $C_{29}H_{50}O_2SeSn$: C, 55.43; H, 8.02. Found: C, 55.64; H, 8.47. For **12b**: IR (film) 3500, 3050, 2940, 2900, 2850, 1680, 1645, 1570, 1450, 1060, 1020, 980, 900, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.23–7.57 (m, 5 H), 3.25–3.45 (m, 3 H), 2.78 (d, 1 H, J = 7.6 Hz), 2.37–2.49 (m, 2 H), 0.77–1.97 (m, 39 H); ^{13}C NMR ($CDCl_3$) δ 217.2, 132.6, 129.8, 129.08, 126.9, 76.8, 54.9, 52.4, 40.5, 39.6, 32.4, 31.8, 30.5, 29.2, 27.5, 25.1, 21.1, 13.7, 10.6. Anal. Calcd for $C_{29}H_{50}O_2SeSn$: C, 55.43; H, 8.02. Found: C, 55.44; H, 8.07.

(2S*,3R*)-3-(Tri-n-butylstannyl)-2-ethenyl-2,5,5-trimethylcyclohexanone (6a). To a solution of β-hydroxy selenide **12a** (126 mg, 0.20 mmol) and Et_3N (0.278 mL, 2.0 mmol) in CH_2Cl_2 (1 mL) at rt was added MsCl (0.093 mL, 1.2 mmol) dropwise. After 5 h, the mixture was diluted with CH_2Cl_2 (15 mL), washed with saturated NaCl (5 mL) and saturated $NaHCO_3$ (2 × 5 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (gradient of 100:1 to 20:1 hexanes/ethyl acetate) to give cyclohexanone **6a** (67 mg, 0.15 mmol, 74%) as a colorless oil: IR (film) 3080, 2920, 2840, 1695, 1635, 1450, 1325, 995, 915, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.13 (dd, J = 17.5, 10.7 Hz, 1 H), 5.14 (d, J = 10.7 Hz, 1 H), 5.01 (d, J = 17.3 Hz, 1 H), 2.53 (d, J = 12.8 Hz, 1 H), 1.85–2.01 (m, 2 H), 0.83–1.58 (series of m, 35 H), 1.14 [s, CH_3(C)CHCH$_2$, 3 H]; ^1H NMR (C_6D_6) δ 6.08 (dd, J = 17.3, 10.7 Hz, 1 H), 5.01 (d, J = 17.6 Hz, 1 H), 4.99 (d, J = 10.4 Hz, 1 H), 2.41 (d, J = 12.8 Hz, 1 H), 1.93–2.08 (m, 2 H), 0.81–1.62 (m, 35 H), 1.37 [s, CH_3(C)CHCH$_2$, 3 H]; ^{13}C NMR ($CDCl_3$) δ 212.7, 141.5, 116.1, 54.1, 52.3, 40.3, 40.1, 36.0, 31.9, 29.2, 27.5, 25.1, 23.3, 13.7, 10.2. Anal. Calcd for $C_{23}H_{44}OSn$: C, 60.68; H, 9.74. Found: C, 60.73; H, 9.63.

(2R*,3R*)-3-(Tri-n-butylstannyl)-2-ethenyl-2,5,5-trimethylcyclohexanone (6b). To a solution of β-hydroxy selenide **12b** (252 mg, 0.40 mmol) and Et_3N (0.556 mL, 4.0 mmol) in CH_2Cl_2 (2 mL) at rt was added MsCl (0.186 mL, 2.4 mmol) dropwise. After 5 h, the mixture was diluted with CH_2Cl_2 (30 mL), washed with saturated NaCl (10 mL) and saturated $NaHCO_3$ (2 × 10 mL) and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (gradient of 100:1 to 20:1 hexanes/ethyl acetate) to give cyclohexanone **6b** (131 mg, 0.29 mmol, 72%) as a colorless oil: IR (film) 3080, 2940, 2840, 1695, 1635, 1455, 1365, 990, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.84 (dd, J = 17.5, 10.9 Hz, 1 H), 5.17 (d, J = 11.0 Hz, 1 H), 5.04 (d, J = 17.6 Hz, 1 H), 2.50 (d, J = 13.2 Hz, 1 H), 1.96–2.05 (m, 2 H), 0.67–1.60 (m, 35 H), 1.28 [s, CH_3(C)CH=CH$_2$, 3 H]; ^1H NMR (C_6D_6) δ 5.99 (dd, J = 17.6, 10.8 Hz, 1 H), 5.10 (dd, J = 10.6, 0.8 Hz, 1 H), 4.98 (d, J = 17.6 Hz, 1 H), 2.25 (d, J = 13.0 Hz, 1 H), 0.81–2.08 (series of m, 37 H), 1.11 [s, CH_3(C)CH=CH$_2$, 3 H]; ^{13}C NMR ($CDCl_3$) δ 214.8, 143.2, 113.6, 53.5, 51.4, 39.9, 39.6, 33.6, 31.9, 29.2, 27.5, 25.3, 20.3, 13.6, 10.3. Anal. Calcd for $C_{23}H_{44}OSn$: C, 60.68; H, 9.74. Found: C, 60.45; H, 10.15.

(1S*,2S*,3R*)-3-(Tri-n-butylstannyl)-1,2-diethenyl-2,5,5-trimethylcyclohexan-1-ol (7a). $CeCl_3$ (197 mg, 0.80 mmol), which had been dried in a vacuum over at 150 °C for 4–6 h, was added to THF (10 mL) that was cooled in an ice bath. The mixture was well stirred at room temperature for 13 h and then cooled to −78 °C. Vinylmagnesium bromide (0.80 mL, 0.80 mmol, 1 M in Et_2O) was added. After 1 h, cyclohexanone **6a** (182 mg, 0.40 mmol) in THF (1 mL) was added dropwise. After 1 h, 10% HOAc (5 mL) was added, and the mixture was allowed to warm to rt, diluted with Et_2O (40 mL), washed with saturated NaCl (2 × 10 mL), saturated $NaHCO_3$ (2 × 10 mL), and saturated NaCl (2 × 10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (20:1 hexanes/ethyl acetate) to give divinylcyclohexanol **7a** (183 mg, 0.37 mmol, 95%) as a colorless oil: IR (film) 3560, 3550, 3080, 2900, 1625, 1450, 1360, 990, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.30 (dd, J = 17.4, 11.0 Hz, 1 H), 5.87 (dd, J = 17.2, 10.7 Hz, 1 H), 5.17 (dd, J = 17.2, 1.1 Hz, 1 H), 4.94–5.09 (m, 3 H), 0.70–2.23 (m, 42 H); ^{13}C NMR ($CDCl_3$) δ 145.2, 142.3, 114.1, 111.5, 77.4, 46.8, 45.8, 39.9, 34.3, 31.1, 31.0, 29.3, 27.7, 27.6, 20.5, 13.7, 10.0. Anal. Calcd for $C_{25}H_{48}OSn$: C, 62.13; H, 10.01. Found: C, 62.27; H, 10.34.

(1S*,2R*,3R*)-3-(Tri-n-butylstannyl)-1,2-diethenyl-2,5,5-trimethylcyclohexan-1-ol (7b). The procedure described in the preparation of **7a** was repeated using $CeCl_3$ (99 mg, 0.40 mmol), THF (5 mL), vinylmagnesium bromide (0.40 mL, 0.40 mmol, 1 M in Et_2O), and cyclohexanone **6b** (91 mg, 0.40 mmol) in THF (1 mL). After 15 min, 10% HOAc (2.5 mL) was added, and the mixture was allowed to warm to rt, diluted with Et_2O (30 mL), washed with saturated NaCl (2 × 10 mL), saturated $NaHCO_3$ (2 × 10 mL), and saturated NaCl (2 × 10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (20:1 hexanes/ethyl acetate) to give **7b** (88 mg, 0.18 mmol, 91%) as a colorless oil: IR (film) 3600, 3550, 3080, 2900, 1630, 1450, 1370, 1000, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.92 (dd, J = 17.3, 10.8 Hz, 1 H), 5.80 (dd, J = 17.8, 10.9 Hz, 1 H), 5.16 (dd, J = 10.9, 1.2 Hz, 1 H), 4.95–5.09 (m, 3 H), 2.30–2.38 (m, 1 H), 0.73–1.76 (m, 41 H); ^{13}C NMR (C_6D_6) δ 146.0, 144.7, 114.2, 112.5, 76.6, 46.6, 44.9, 40.4, 34.7, 34.6, 31.5, 29.8, 29.2, 28.1, 20.4, 14.0, 10.6. Anal. Calcd for $C_{25}H_{48}OSn$: C, 62.13; H, 10.01. Found: C, 62.48; H, 10.46.

(1R*,7S*)- and (1S,7S*)-3,3,6-Trimethylbicyclo[5.3.0]dec-5-en-1-ol (10 and 9). To a suspension of KH (0.458 g, 35% in oil, 4.0 mmol, washed 3 × 2 mL with hexanes) in Et_2O (16 mL) at RT was added a mixture of **7a,b** (194 mg, 0.4 mmol) in Et_2O (2 mL) dropwise. After 5 h, the mixture was cooled to −78 °C, quenched with absolute EtOH (5 mL), diluted with Et_2O (20 mL) and saturated NH_4Cl (10 mL), washed with saturated NaCl (2 × 10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (50:1 hexanes/ethyl acetate) to give the *trans*-hydroazulene **10** (44 mg, 0.23 mmol, 57%) and the *cis*-hydroazulene **9** (15 mg, 0.08 mmol, 19%) as colorless oils. For **9**: IR (film) 3590, 3470, 3010, 2920, 1630, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.48–5.57 (m, 1 H), 2.63 (t, J = 8.0 Hz, *CH*C(OH), 1 H), 1.18–2.19 (series of m, 11 H), 1.73 (s, 3 H), 1.11 (s, 3 H), 0.89 (s, 3 H); ^1H NMR (pyridine-d_5) δ 5.65–5.57 (m, 1 H), 2.97 (t, J = 8.6 Hz, *CH*C(OH), 1 H), 1.00–2.61 (series of m, 11 H), 1.74 (s, 3 H), 1.34 (s 3 H), 0.93 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.44, 123.01, 82.25, 53.82, 49.53, 44.15, 38.78, 32.54, 31.71, 29.84, 28.92, 24.16, 22.03; MS m/z (M^+) calcd 194.1, obsd 194.1. Anal. Calcd for $C_{13}H_{22}O$: C, 80.36; H, 11.41. Found: C, 80.26; H, 11.39. For **10**: IR (film) 3620–3300, 3030, 2940, 1640 (w), 1440, 1360, 1260, 1025, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.64–5.72 (m, 1 H), 2.72 (t, J = 9.6 Hz, *CH*C(OH), 1 H), 2.17–2.26 (m, 1 H), 1.17–2.01 (series of m, 10 H), 1.78 (s, 3 H), 1.04 (s, 3 H), 0.90 (s, 3 H); ^1H NMR (pyridine-d_5) δ 5.65–5.71 (m, 1 H), 2.61–2.71 (m, *CH*C(OH), 1 H), 1.07–2.34 (m, 11 H), 1.87 (s, 3 H), 1.28 (s, 3H), 0.88 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.0, 125.5, 81.0, 56.0, 50.8, 42.4, 40.4, 35.1, 31.7, 28.2, 26.9, 23.2, 22.3. Anal. Calcd for $C_{13}H_{22}O$: C, 80.36; H, 11.41. Found: C, 80.27; H, 11.44.

Reaction of Cyclodecenone 8 with n-Bu$_4$NF. To a suspension of KH (1.72 g, 35% in oil, 15.0 mmol, washed with hexane) in Et_2O (60 mL) at rt was added a mixture of **7a,b** (725 mg, 1.50 mmol) in Et_2O (2 mL) dropwise. After 2 h, the mixture was cooled to −78 °C, quenched with absolute EtOH (10 mL), diluted with pentane (80 mL) and saturated NH_4Cl (40 mL), washed with saturated NaCl (2 × 30 mL), and dried over $MgSO_4$. The filtrate was concentrated to give a residue whose IR spectrum showed a carbonyl stretch and no hydroxyl group. To this residue was added THF (30 mL) and *n*-Bu_4NF (3.0 mL, 3.0 mmol, 1.0 M in THF) at room temperature. After 5 h, the solution was filtered through silica gel. The filtrate was concentrated and purified by flash chromatography (10:1 hexanes/ethyl acetate) to give the *cis*-hydroazulene **9** (235 mg, 1.21 mmol, 80%) as a colorless oil.

(1S*,2S*,3R*)-3-(Tri-n-butylstannyl)-2-ethenyl-2,5,5-trimethyl-1-(1-methylethenyl)cyclohexan-1-ol (13a). The procedure described in the preparation of **7a** was repeated using $CeCl_3$ (935 mg, 3.8 mmol), THF (15 mL), isopropenylmagnesium bromide (6.0 mL, 3.8 mmol, 0.63 M in THF, prepared by slowly adding isopropenyl bromide to magnesium at 25 °C), and cyclohexanone **6a** (432 mg, 0.95 mmol) in THF (1 mL). After 1 h, 10% HOAc (30 mL) was added, and the mixture was allowed to warm to rt, diluted with Et_2O (60 mL), washed with saturated NaCl (3 × 10 mL), saturated $NaHCO_3$ (3 × 10 mL), and saturated NaCl (10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give divinylcyclohexanol **13a** (426 mg, 0.86 mmol, 90%) as a colorless oil: IR (film) 3600, 3500, 3080, 2920, 1625, 1450, 1370, 1000, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.33 (dd, J = 17.3, 11.0 Hz, 1 H), 4.96–5.02 (m, 3 H), 4.90 (s, 1 H), 2.28 (dd, J = 14.6, 3.2 Hz, 1 H), 1.81–2.06 (m, 2 H), 1.71 (s, 3 H), 0.61–1.44 (m, 39 H); ^{13}C NMR ($CDCl_3$) δ 151.1, 143.2, 113.2, 112.6, 79.9, 46.0, 45.9, 40.0, 34.8, 32.4, 31.5, 29.3, 27.8, 27.6, 22.8, 19.8, 13.7, 10.2. Anal. Calcd for $C_{26}H_{50}OSn$: C, 62.79; H, 10.13. Found: C, 63.00; H, 10.41.

(1S*,2R*,3R*)-3-(Tri-n-butylstannyl)-2-ethenyl-2,5,5-trimethyl-1-(1-methylethenyl)cyclohexan-1-ol (13b). The procedure described in the preparation of **7a** and **13a** was repeated using $CeCl_3$ (468 mg, 1.9 mmol), THF (10 mL, stirred at 25 °C for 17 h), isopropenylmagnesium bromide (4.0 mL, 1.9 mmol, 0.48 M in THF), and cyclohexanoneone **6b** (216 mg, 0.47 mmol) in THF (1 mL). After 1 h, 10% HOAc (15 mL) was added, and

the mixture was allowed to warm to rt, diluted with Et_2O (40 mL), washed with saturated NaCl (3 × 10 mL), saturated $NaHCO_3$ (3 × 10 mL), and saturated NaCl (10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give divinylcyclohexanol **13b** (186 mg, 0.37 mmol, 80%) as a colorless oil: IR (film) 3600–3480, 3080, 2920, 1625, 1450, 1370, 1175, 1010, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.94 (dd, J = 17.8, 10.9 Hz, 1 H), 4.93–5.14 (m, 3 H), 4.74 (s, 1 H), 2.37 (dd, J = 14.3, 2.9 Hz, 1 H), 1.95 (d, J = 14.7 Hz, 1 H), 1.75 (s, 3 H), 0.72–1.71 (m, 40 H); ^{13}C NMR ($CDCl_3$) δ 151.0, 146.2, 113.9, 113.1, 79.2, 46.7, 45.0, 39.8, 34.7, 31.6, 29.2, 29.2, 27.6 (two peaks), 22.5, 21.0, 13.7, 10.3. Anal. Calcd for $C_{26}H_{50}OSn$: C, 62.79; H, 10.13. Found: C, 63.11; H, 10.52.

(2*S,7*R**)-7-(Tri-*n*-butylstannyl)-2,6,9,9-tetramethylcyclodec-5-en-1-one (4a).** To a suspension of KH (160 mg, 26% in oil, 1.0 mmol, washed 3 × 2 mL with hexanes) in Et_2O (8 mL) at rt was added divinylcyclohexanol **13a** (97 mg, 0.2 mmol) in Et_2O (0.5 mL) dropwise. After 2.5 h, the mixture was cooled to −78 °C, quenched with absolute EtOH (3 mL), diluted with Et_2O (30 mL), washed with saturated NaCl (3 × 10 mL), and dried over $MgSO_4$. The filtrate was concentrated to give crude cyclodecenone **4a** (93 mg, 96%): IR (film) 3010, 2860, 1670, 1625, 1430, 1355, 1050, 890, 850, 720 cm^{-1}; ^1H NMR (C_6D_6) δ 5.17 (dd, J = 10.0, 4.4 Hz, 1 H), 0.79–2.85 (m, 49 H); ^{13}C NMR (C_6D_6) δ 212.3, 140.2, 121.2, 48.4, 47.4, 40.0, 36.0, 34.3, 32.0, 31.0, 29.7, 29.3, 27.9, 25.0, 20.1, 16.3, 14.0, 9.19. This material was unstable in $CDCl_3$, and was used directly in the next step.

(1*R,7*S**,10*S**)-3,3,6,10-Tetramethylbicyclo[5.3.0]dec-5-en-1-ol (3a).** To the crude cyclodecenone prepared as described above from divinylcyclohexanol **13a** (500 mg, 1 mmol) in THF (10 mL) at rt was added sodium naphthalenide[16] (5.0 mL, 7.5 mmol, 1.5 M in THF) dropwise. After 15 min, the mixture was diluted with Et_2O (30 mL), washed with 0.1 N HCl (50 mL), saturated NaCl (2 × 15 mL), and saturated $NaHCO_3$ (2 × 15 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *cis,trans*-hydroazulene **3a** (106 mg, 0.51 mmol, 51%) and the *cis,cis*-hydroazulene **3b** (11 mg, 0.05 mmol, 5%). For **3a**: IR (film) 3460, 3040, 2940, 1660, 1450, 1370, 1355, 1040, 965, 825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.44–5.51 (m, 1 H), 2.47 (dd, J = 12.2, 8.2 Hz, 1 H), 1.99 (d, J = 7.0 Hz, 1 H), 1.20–1.94 (m, 9 H), 1.75 (s, 3 H), 1.11 (s, 3 H), 0.93 (s, 3 H), 0.84 (d, J = 6.7 Hz, 3 H); ^1H NMR (pyridine-d_5) δ 5.52–5.59 (m, 1 H), 2.76 (dd, J = 11.1, 8.5 Hz, 1 H), 2.31 (dd, J = 14.3, 8.1 Hz, 1 H), 1.06–2.10 (m, 9 H), 1.76 (s, 3 H), 1.38 (s, 3 H), 0.98 (s, 3 H), 0.95 (d, J = 6.9 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.0, 123.0, 81.3, 55.8, 47.8, 44.4, 40.2, 34.4, 31.7, 28.8, 27.7, 26.6, 24.9, 13.6. Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.57; H, 11.28.

(1*S,7*S**,10*S**)-3,3,6,10-Tetramethylbicyclo[5.3.0]dec-5-en-1-ol (14).** To the crude cyclodecenone **4a** (prepared from 100 mg, 0.20 mmol of divinylcyclohexanol **13a** as described above) in THF (8 mL) at rt was added CF_3CO_2H (0.031 mL, 0.4 mmol) dropwise. After 2 h, the mixture was diluted with Et_2O (20 mL), washed with saturated NaCl (2 × 5 mL) and saturated $NaHCO_3$ (2 × 5 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *trans,cis*-hydroazulene **14** (27 mg, 0.13 mmol, 65%) as a yellowish oil: IR (film) 3620–3400, 3080, 3020, 2920, 1635, 1440, 1370, 1355, 1140, 900, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.63–5.70 (m, 1 H), 2.90 (t, J = 9.3 Hz, *CH*C(OH), 1 H), 2.19 (dd, J = 14.2, 5.2 Hz, 1 H), 1.11–2.02 (m, 9 H), 1.77 (d, J = 1.0 Hz, 3 H), 1.03 (s, 3 H), 0.93 (d, J = 6.5 Hz, 3 H), 0.90 (s, 3 H); ^1H NMR (pyridine-d_5) δ 5.64–5.73 (m, 1 H), 2.82–2.91 (m, *CH*C(OH), 1 H), 0.92–2.32 (m, 10 H), 1.84 (s, 3 H), 1.23 (s, 3 H), 1.07 (d, J = 6.2 Hz, 3 H), 0.91 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.8, 125.5, 80.7, 53.7, 50.1, 46.3, 40.3, 34.9, 31.6, 30.2, 27.1, 24.6, 23.8, 12.9. Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.94; H, 11.15.

Reaction of Cyclodecenone 4a with $SnCl_4$. To the crude cyclodecenone **4a** (prepared from 100 mg, 0.20 mmol of divinylcyclohexanol **13a** as described above) in THF (8 mL) at −78 °C was added $SnCl_4$ (0.40 mL, 0.40 mmol, 1 M in CH_2Cl_2) dropwise. After 2 h, the mixture was diluted with Et_2O (20 mL), washed with saturated $NaHCO_3$ (10 mL) and saturated NaCl (10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *cis,trans*-hydroazulene **3a** (22 mg, 0.11 mmol, 53%) and the *trans,cis*-hydroazulene **14** (4 mg, 0.02 mmol, 10%).

Reaction of Cyclodecenone 4a with *n*-Bu_4NF. To a crude cyclodecenone **4a** (prepared from 100 mg, 0.20 mmol of divinylcyclohexanol **13a** as described above) in THF (8 mL) at rt was added *n*-Bu_4NF (0.40 mL, 0.40 mmol, 1.0 M in THF) dropwise. After 16 h, the mixture was filtered through a plug of silica gel. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *trans,cis*-hydroazulene **14** (22 mg, 0.11 mmol, 52%) and the *cis,trans*-hydroazulene **3a** (5 mg, 0.024 mmol, 12%).

Reaction of Cyclodecenone 4a with SmI_2. To SmI_2 (0.40 mmol, prepared from Sm and CH_2I_2)[17] in THF (2 mL) at rt was added crude cyclodecenone **4a** (prepared as described above from 98mg, 0.2 mmol of divinylcyclohexanol **13a**) in THF (0.5 mL) dropwise. After 3 h, the mixture was diluted with Et_2O (30 mL), washed with saturated NaCl (2 × 10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *trans,cis*-hydroazulene **14** (26 mg, 0.13 mmol, 62%) and the *cis,trans*-hydroazulene **3a** (5 mg, 0.024 mmol, 12%).

Africanol (1). To a solution of *cis,trans*-hydroazulene **3a** (42 mg, 0.20 mmol) in dichloroethane (1 mL) at 0 °C was added dropwise Et_2Zn (1.0 mL, 1.0 mmol, 1 M in dichloroethane) and then CH_2I_2 (0.162 mL, 2.0 mmol). After 10 min, saturated NH_4Cl (4 mL) was added slowly. The mixture was diluted with Et_2O (30 mL), washed with saturated NaCl (2 × 15 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (20:1 hexanes/ethyl acetate) to give africanol (1)[2b,3c] (36 mg, 0.16 mmol, 81%) as a colorless crystalline solid: mp 45–46 °C; IR (CCl_4) 3595, 3480, 3050, 2940, 1450, 1375, 1355, 1155, 1095, 1010, 980, 940, 885 cm^{-1}; ^1H NMR (C_6D_6) δ 1.25–1.99 (m, 11 H), 1.22 (s, 3 H), 1.02 (s, 3 H), 0.85 (s, 3 H), 0.76 (d, J = 7.3 Hz, 3 H), 0.58–0.74 (m, 1 H), 0.45 (dd, J = 8.5, 3.8 Hz, 1 H), 0.16 (t, J = 4.4 Hz, 1 H); ^{13}C NMR (C_6D_6) δ 86.7, 56.1, 50.2, 45.2, 40.6, 34.4, 32.2, 31.8, 31.6, 26.3, 23.9, 23.0, 21.9, 18.3, 15.4; ^1H NMR ($CDCl_3$) δ 1.24–2.10 (m, 11 H), 1.11 (s, 3 H), 1.01 (s, 3 H), 0.95 (s, 3 H), 0.88 (d, J = 7.3 Hz, 3 H), 0.64–0.79 (m, 1 H), 0.47 (dd, J = 8.4, 3.9 Hz, 1 H), 0.15 (t, J = 4.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 87.3, 55.9, 50.1, 45.1, 40.3, 34.3, 32.0, 31.7, 31.4, 26.0, 23.6, 22.9, 21.5, 18.2, 15.3.

(1*R,7*S**,10*R**)-3,3,6,10-Tetramethylbicyclo[5.3.0]dec-5-en-1-ol (3b).** To a suspension of KH (1.14 g, 35% in oil, 10 mmol, washed 3 × 2 mL with hexanes) in Et_2O (40 mL) at room temperature was added divinylcyclohexanol **13b** (497 mg, 1 mmol) in Et_2O (2 mL) dropwise. After 2 h, the mixture was cooled to −78 °C, quenched with absolute EtOH (5 mL), diluted with Et_2O (40 mL), washed with saturated NaCl (2 × 20 mL), and dried over $MgSO_4$. The filtrate was concentrated to give a residue whose IR spectrum showed a carbonyl stretch and no hydroxyl group. To this residue in THF (16 mL) at rt was added *n*-Bu_4NF (2.0 mL, 2.0 mmol, 1.0 M in THF) dropwise. After 3 h, the mixture was filtered through silica gel. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *cis,cis*-hydroazulene **3b** (151 mg, 0.73 mmol, 73%) as a colorless oil: IR (film) 3500, 3030, 2930, 2860, 1620, 1450, 1370, 1360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.51–5.58 (m, 1 H), 2.79 (t, J = 8.0 Hz, *CH*C(OH), 1 H), 2.21 (dd, J = 13.3, 7.6 Hz, 1 H), 1.23–2.05 (m, 9 H), 1.72 (s, 3 H), 1.08 (s, 3 H), 0.92 (d, J = 6.3 Hz, 3 H), 0.87 (s, 3 H); ^1H NMR (pyridine-d_5) δ 5.57–5.66 (m, 1 H), 3.10 (t, J = 7.1 Hz, *CH*C(OH), 1 H), 2.50 (dd J = 13.3, 7.5 Hz, 1 H), 1.35–2.01 (m, 9 H), 1.74 (s, 3 H), 1.28 (s, 3 H), 1.12 (d, J = 6.2 Hz, 3 H), 0.93 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.2, 122.8, 82.4, 53.3, 47.3, 45.1, 38.2, 32.0, 31.3, 30.9, 30.9, 26.6, 23.3, 12.5. Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.57; H, 11.59.

Reaction of Cyclodecenone 4b with $Na/C_{10}H_8$. To crude cyclohexanone **4b** (prepared from 50 mg, 0.1 mmol of divinylcyclohexanol **13b** as described above) in THF (1 mL) at rt was added sodium naphthalenide[16] (1.0 mL, 0.75 mmol, 0.75 M in THF) dropwise. After 15 min, the mixture was diluted with Et_2O (15 mL), washed with 0.1 N HCl (5 mL), saturated NaCl

(16) Pattenden, G.; Robertson, G. M. *Tetrahedron* **1985**, *41*, 4001–4011.

(17) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1991**, *56*, 4112–4120.

(2 × 5 mL), and saturated $NaHCO_3$ (5 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (10:1 hexanes/ethyl acetate) to give the *cis,cis*-hydroazulene **3b** (15 mg, 0.07 mmol, 70%) as a colorless oil.

Reaction of Cyclodecenone 4b with SmI_2. To SmI_2 (0.40 mmol, prepared from Sm and CH_2I_2)[17] in THF (2 mL) at rt was added the crude cyclodecenone **4b** (prepared as described above from 100 mg, 0.2 mmol, of divinylcyclohexanol **13b**) in THF (0.5 mL) dropwise. After 30 min, the mixture was diluted with Et_2O (30 mL), washed with saturated NaCl (2 × 10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *cis,cis*-hydroazulene **3b** (27 mg, 0.13 mmol, 64%).

(1*S,7*S**,10*R**)-3,3,6,10-Tetramethylbicyclo[5.3.0]dec-5-en-1-ol (15).** To crude cyclodecenone **4b** (prepared as described above from 100 mg, 0.2 mmol of divinylcyclohexanol **13b**) in THF (8 mL) at rt was added CF_3CO_2H (0.062 mL, 0.080 mmol) dropwise. After 3 h, the mixture was diluted with Et_2O (30 mL), washed with saturated NaCl (2 × 10 mL) and saturated $NaHCO_3$ (2 × 10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *trans,trans*-hydroazulene **15** (14 mg, 0.077 mmol, 33%) and the *cis,cis*-hydroazulene **3b** (16 mg, 0.077 mmol, 38%). For **15**: IR (film) 3620–3340, 3030, 2940, 1640–1610 (very weak), 1440, 1370, 1360, 1260, 1040, 960, 825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.65–5.72 (m, 1 H), 2.76 (t, J = 9.4 Hz, 1 H), 1.11–2.25 (m, 9 H), 1.78 (s, 3 H), 1.05 (s, 3 H), 0.93 (s, 3 H), 0.92 (d, J = 6.8 Hz, 3 H); ^1H NMR (pyridine-d_5) δ 5.65–5.72 (m, 1 H), 2.74 (t, J = 9.3 Hz, 1 H), 1.01–2.33 (m, 9 H), 1.87 (s, 3 H), 1.30 (s, 3 H), 0.93 (s, 3 H), 0.91 (d, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.3, 125.2, 81.5, 51.6, 50.0, 46.6, 40.2, 35.5, 33.1, 31.1, 27.4, 26.1, 23.2, 17.4. Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.88; H, 12.05.

Reaction of Cyclodecenone 4b with $SnCl_4$. To crude cyclodecenone **4b** (prepared as described above from 50 mg, 0.10 mmol of divinylcyclohexanol **13b**) in THF (4 mL) at −78 °C was added $SnCl_4$ (0.20 mL, 0.20 mmol, 1 M in CH_2Cl_2) dropwise. After 3 h, the mixture was diluted with Et_2O (30 mL), washed with saturated $NaHCO_3$ (10 mL), saturated NaCl (2 × 5 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (30:1 hexanes/ethyl acetate) to give the *cis,cis*-hydroazulene **3b** (9 mg, 0.04 mmol, 43%) and the *trans,trans*-hydroazulene **15** (3 mg, 0.01 mmol, 14%).

Isoafricanol (2). To a solution of *cis,cis*-hydroazulene **3b** (105 mg, 0.50 mmol) in dichloroethane (2.5 mL) at 0 °C was added Et_2Zn (2.5 mL, 2.5 mmol, 1 M in dichloroethane). Then CH_2I_2 (0.405 mL, 5 mmol) was added dropwise. After 30 min, saturated NH_4Cl (5 mL) was added slowly. The mixture was diluted with Et_2O (40 mL), washed with saturated NaCl (2 × 10 mL), and dried over $MgSO_4$. The filtrate was concentrated and purified by flash chromatography (20:1 hexanes/ethyl acetate) to give isoafricanol (**2**)[2b] (87 mg, 0.39 mmol, 78%) as a colorless oil: IR (film) 3600, 3450, 3040, 2900, 1445, 1370, 1350 cm^{-1}; ^1H NMR (C_6D_6) δ 0.46–1.91 (m, 9 H), 1.43 (s, 2 H), 1.21 (s, 3 H), 0.98 (s, 3 H), 0.81 (d, J = 5.7 Hz, 3 H), 0.80 (s, 3 H), 0.38 (dd, J = 8.6, 4.0 Hz, 1 H), 0.12 (t, J = 4.4 Hz, 1 H); ^{13}C NMR (C_6D_6) δ 85.2, 54.5, 46.5, 46.0, 41.2, 34.2, 31.8, 31.6, 31.3, 23.8, 23.0, 22.2, 21.3, 18.8, 12.4; ^1H NMR ($CDCl_3$) δ 1.21–1.90 (m, 11 H), 1.11 (s, 3 H), 0.97 (s, 3 H), 0.92 (s, 3 H), 0.90 (d, J = 6.3 Hz, 3 H), 0.58–0.75 (m, 1 H), 0.40 (dd, J = 8.3, 4.1 Hz, 1 H), 0.14 (t, J = 4.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 85.7, 53.8, 46.4, 45.6, 40.9, 34.0, 31.6, 31.3, 31.1, 23.5, 22.6, 22.1, 20.9, 18.7, 12.3.

Acknowledgment. We thank the National Institutes of Health and the Robert A. Welch Foundation for their generous support and Professor William Smith (Department of Chemistry, Texas Christian University) for carrying out relevant molecular mechanics calculations. Purchase of the C,H,N analyzer through a grant from the Defense Advanced Research Projects Agency monitored by the Office of Naval Research is gratefully acknowledged. We would also like to thank one reviewer for helpful and encouraging comments.