over several minutes. The aqueous reaction mixture was extracted with CH_2Cl_2 (3 × 15 mL). The organic layer was dried and evaporated to obtain 37 mg (62%) of an oil, which solidified in part on standing. *N*-Chloropiperidine, prepared by shaking piperidine with excess NaOCl or by the action of *N*-chlorosuccinimide on piperidine,[25] was also a liquid that solidified on standing. The NMR spectra, TLC, and mass spectra of all three samples were identical: NMR ($CDCl_3$) δ 1.18–1.82 (m, 6 H), 3.0 (distorted t, 4 H); MS, *m/z* 121 and 119, 120 and 118, 84, 55 and 42; TLC ($CHCl_3$) R_f = 0.59; unstained by I_2. The reaction was repeated and the reaction mixture acidified at the end with 3 mL of 1 N HCl. $BaCO_3$ from the CO_2 traps weighed 58 mg (59% after correcting for a blank). At times the NMR spectrum of the crude reaction product had an A_2B_2 pattern, presumably the result of a cyclopropane-ring-opening reaction.

Reaction of 6-*cis*-d_2 with Hypochlorite. To 20 mg (0.14 mmol) of **6**-d_2[8] in a flask sealed with a septum was injected a solution of LiOCl (65 mg, 0.34 mmol) in 1 mL of water. The head-space gas was analyzed for ethylene-1,2-d_2 by infrared spectroscopy (see the section on 1-(*N*-methylamino)cyclopropanecarboxylic acid-2,3-d_2 above). Only ethylene-*cis*-1,2-d_2 (842 cm^{-1}) was observed.[23]

Reaction of 6 with Alkaline Peroxide. Into a solution of 70 mg (0.5 mmol) of **6** and 210 mg (2.5 mmol) of $NaHCO_3$ in 4 mL of water was injected 0.3 mL (3 mmol) of 30% H_2O_2. The solution was stirred for 2 h. The gas evolved (4.5 mL) was a mixture of ethylene and CO_2, according to GC. The reaction mixture was extracted with EtOAc (3 × 10 mL) to obtain 40 mg of an oil, which was, according to NMR, a mixture of *N*-acryloylpiperidine (**10**, prepared independently by the action of piperidine on acryloyl chloride) and *N*-(3-hydroxypropionyl)piperidine (**2g**, prepared by the action of piperidine on β-propiolactone). NMR ($CDCl_3$): **10** δ 1.57 (br s, 6 H), 3.5 (distorted t, 4 H), 5.2–6.7 [ABX vinyl pattern 5.2–5.68 (dd, 1 H), 6.08–6.33 (distorted dd, 1 H), 6.4–6.7 (distorted dd, 1 H)]; **2g** δ 1.58 (br s, 6 H), 2.48 (t, *J* = 5.4 Hz, 2 H), 3.3 (distorted t, 2 H), 3.52 (distorted t, 2 H), 3.82 (t, *J* = 5.4 Hz, 2 H).

N-Substituted 3-Hydroxypropanamides 2b, 2c, and 2g.[24] A solution of 72 mg (1 mmol) of β-propiolactone in 2 mL of benzene was added dropwise to 1 mmol of amine, cooled in an ice bath. (In the case of methylamine, the vapors were trapped at −78 °C and excess amine was used.) The reaction mixture was stirred overnight at room temperature. Benzene was removed, and the residual oil was redissolved in EtOAc, washed with 1 N HCl and water, and dried. Solvent was removed to isolate the hydroxy amides in 70–80% yield.

Acknowledgment. We acknowledge with gratitude the help of Dr. Dennis Clouthier in obtaining spectra on the BOMEM FTIR spectrometer.

Registry No. **1b**, 99324-92-2; **1b**·HCl, 99324-91-1; **1b**-d_2, 119111-68-1; *N*-BOC-**1b**, 119145-87-8; **1c**, 119111-62-5; **1c**·HCl, 119111-75-0; **1c** (methyl ester), 119111-70-5; **1d**, 119111-63-6; **1e**, 119111-64-7; **1e**-d_2, 119111-71-6; **1f**, 119111-65-8; **1g**, 765-30-0; **1h**, 22936-83-0; **1i**, 72784-43-1; **1i**·HCl, 72784-42-0; **1i** (Schiff base), 119111-69-2; **1j**, 119111-66-9; *N*-chloro-**1j**, 119111-74-9; **2a**, 109-78-4; **2b**, 6830-81-5; **2c**, 19340-82-0; **2d**, 590-90-9; **2g**, 86452-58-6; **3**, 100-52-7; **4**, 100-46-9; **5**, 119111-61-4; **6**, 27161-21-3; **6**-*cis*-d_2, 119111-76-1; **10**, 10043-37-5; ACC, 22059-21-8; *N*-BOC-ACC, 88950-64-5; ACC-d_2, 119238-02-7; ACC-d_2 (methyl ester), 119111-72-7; 1-methylcyclopropanecarboxylic acid, 6914-76-7; 1-methylcyclopropanecarboxamide, 15910-91-5; *N*-bromo-1-methylcyclopropanecarboxamide, 119111-67-0; diiodopentane, 628-77-3; methyl *cis*-2,3-dideuterio-1-(1-piperidino)cyclopropanecarboxylate, 119111-73-8; ethylene, 74-85-1; acrylonitrile, 107-13-1; β-propiolactone, 57-57-8; *cis*-ethylene-1,2-d_2, 2813-62-9; *N*-chloropiperidine, 2156-71-0; piperidine, 110-89-4; acryloyl chloride, 814-68-6; methylamine, 74-89-5.

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Synthesis, Absolute Stereochemistry, and Circular Dichroism of Chiral 1,8a-Dihydroazulene Derivatives

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A model compound, (8a*S*)-(+)-1,8a-dihydro-8a-methylazulene (**6**), was synthesized from *trans*-ketone (1*S*,3a*R*,8a*S*)-(**9a**) in order to determine the absolute stereostructure of the liverwort sesquiterpene (+)-1,8a-dihydro-3,8-dimethylazulene (**1**) by CD spectroscopy. The CD Cotton effects of compound **6** were stronger and closer, in intensity, to those of the natural product **1** than those of the previous model compounds **4** and **5**. Another model compound **7** also showed similar CD Cotton effects to those of **1**. Therefore, the present CD data experimentally establish the absolute configuration of (+)-**1** previously predicted to be 8a*S* on the basis of theoretical CD spectra. The absolute configuration was also corroborated by an X-ray crystallographic analysis of compound (+)-**10**. The present CD and X-ray studies have thus experimentally validated the methodology for determining absolute stereostructures of twisted π-electron systems on the basis of the theoretical CD spectra calculated by the π-electron SCF-CI-DV MO method.

Theoretical calculation of CD spectra of twisted and conjugated π-electron systems by the π-electron SCF-CI-dipole velocity molecular orbital method[2–5] enables one to predict the absolute stereostructures of various natural and synthetic chiral organic compounds[6–11] in a nonempirical manner. For example, we have determined the absolute stereochemistry of (+)-halenaquinol and (+)-halenaqui-

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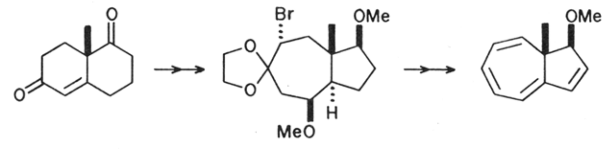


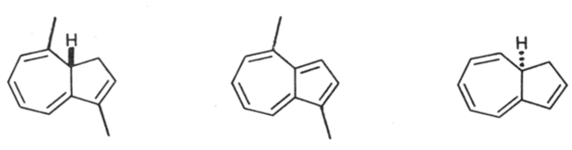
(8aS)-(+)-8 (1S,3aR,4S,7R,8aS)- (1S,8aS)-(+)-4

Chem. Correl. (+)-10, X-ray CD

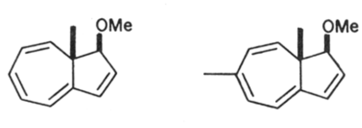
Figure 1. Chemical correlation of the absolute stereochemistry of Wieland–Miescher ketone (8a*S*)-(+)-**8**, bromide (1*S*,3a*R*,4*S*,7*R*,8a*S*)-(+)-**10**, and 1,8a-dihydroazulene derivative (1*S*,8a*S*)-(+)-**4**.

none,[7,11] troponoid spiro compounds,[8] and dissymmetric 4,4′-biphenanthrylidene olefins,[9] by theoretical calculation of the CD spectra of pertinent derivatives.

In addition, we reported the determination of the absolute configuration of (+)-1,8a-dihydro-3,8-dimethylazulene (**1**),[6] a trinorsesquiterpenoid isolated from a liverwort as an extremely unstable biosynthetic precursor to 1,4-dimethylazulene (**2**).[12] The calculated CD curve of a model compound (**3**) with 8a*R* absolute configuration was similar in the shape and position of Cotton effects, but opposite in sign to the observed CD spectrum for the twisted and conjugated π-electron system of natural product **1**. The absolute configuration of (+)-**1** was therefore assigned to be 8a*S*.[6]

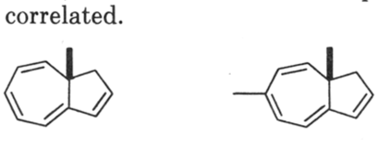


(8aS)-(+)-1 2 (8aR)-3



(1S,8aS)-(+)-4 (1S,8aS)-(+)-5

The 8a*S* absolute configuration of **1** was confirmed experimentally by synthesis of two stable model compounds (1*S*,8a*S*)-(+)-(**4**) and (1*S*,8a*S*)-(+)-(**5**) from the Wieland–Miescher ketone (8a*S*)-(+)-(**8**) (Figure 1).[6] The observed CD spectra of the model compounds were similar to those of natural product **1** in the sign, shape, and position of Cotton effects. However, the observed Δε values were about half of those of **1**. The difference may be caused by the extra chirality of the methoxyl group. This problem prompted us to synthesize model compounds (8a*S*)-(+)-**6** and (8a*S*)-(+)-**7** lacking the methoxyl group. Here, we report the synthesis, absolute stereochemistry, and circular dichroism of **6** and **7** and also describe the X-ray crystallographic determination of the absolute stereostructure of compound **10**, to which the model compounds were chemically correlated.



(8aS)-(+)-6 (8aS)-(+)-7

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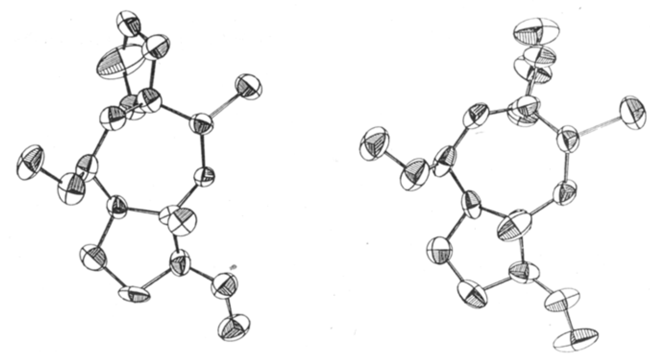


Figure 2. ORTEP drawing of the absolute stereostructures of the two crystallographically independent molecules of (1*S*,3a*R*,4*S*,7*R*,8a*S*)-(+)-**10** contained in an asymmetric unit.

Results and Discussion

Absolute Stereostructures of 1,8a-Dihydroazulene Derivatives As Determined by the X-ray Crystallographic and Chemical Correlation Methods. In addition to the previous determination[6] of the absolute configurations of chiral 1,8a-dihydroazulene derivatives on the basis of the CD spectroscopic studies of (+)-**4** and (+)-**5** and the chemical correlation to (8a*S*)-(+) Wieland–Miescher ketone **8**, their absolute stereostructures were further established by the X-ray crystallographic studies of a synthetic intermediate, bromide (+)-**10**, for the dihydroazulenes (Figure 1).

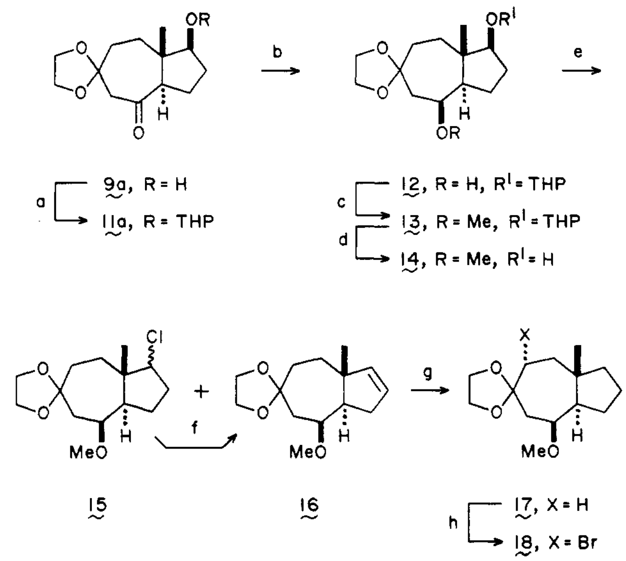
Bromide (+)-**10** forms clear prisms, when recrystallized from diethyl ether: mp 102 °C; $[\alpha]_D$ +49.6° (*c* 1.003, $CHCl_3$). The crystals were found to be orthorhombic and the space group to be $P2_12_12_1$: a = 15.139 Å, b = 22.597 Å, c = 9.268 Å, vol = 3176.8 Å^3. The observed value of density, ρ(obsd) = 1.443 g/cm^3, indicated that one asymmetric unit contained two crystallographically independent molecules of bromide **10**: ρ(calcd) = 1.452 g/cm^3. The crystal structure was solved by the direct method and by the successive Fourier synthesis. The least-squares refinement of positional and thermal parameters, including anomalous scattering factors, led to the final convergence with R = 0.0427. The relative stereochemistry obtained was in agreement with that obtained from the ^{1}H NMR spectral data, and the absolute configuration of bromide (+)-**10** was determined to be 1*S*,3a*R*,4*S*,7*R*,8a*S* as illustrated in Figure 2. The present X-ray crystallographic results have thus established the absolute configurations of chiral 1,8a-dihydroazulenes, (+)-**4**, (+)-**5**, (+)-**6**, and (+)-**7**.

Synthesis of 1,8a-Dihydroazulene Derivatives (+)-6 and (+)-7. We previously reported the synthesis of chiral 1,8a-dihydroazulenes (+)-**4** and (+)-**5**[6] via ketone (1*S*,3a*R*,8a*S*)-**9a**,[13] which was prepared from (8a*S*)-(+) Wieland–Miescher ketone **8**. The present target molecules, (+)-**6** and (+)-**7**, were similarly synthesized by starting from the key intermediate (1*S*,3a*R*,8a*S*)-**9a** as shown in Schemes I and II.

Ketone **9** containing trans isomer **9a** as a major component[13] was converted to the tetrahydropyranyl (THP) ether, which was chromatographed on silica gel, giving the major product, *trans*-(1*S*,3a*R*,8a*S*)-**11a**, and the minor one, *cis*-(1*S*,3a*S*,8a*S*)-**11b** (Scheme I). Reduction of ketone **11a** with $LiAlH_4$ afforded alcohol **12**. After the hydroxyl group

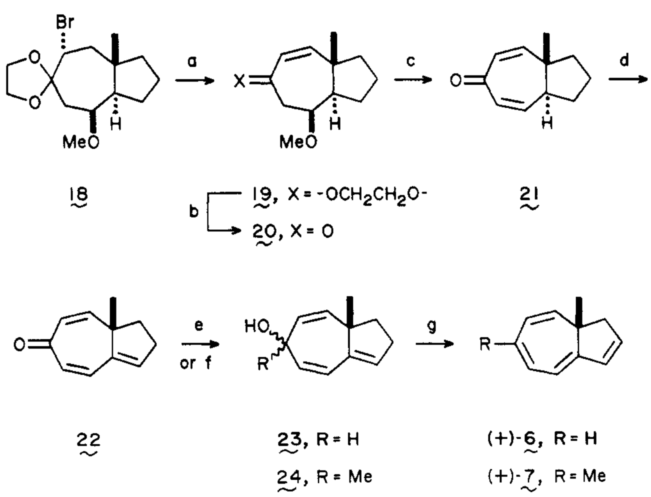
(13) For the original synthesis of racemic ketone **9** and the discussion on the ring junction, see Heathcock, C. H.; DelMar, E.; Graham, S. L. *J. Am. Chem. Soc.* **1982**, *104*, 1907. Their assignment of the relative stereochemistry of the ring junction was now directly evidenced by the X-ray studies of compound (+)-**10**.

Scheme I[a]



[a] (a) 3,4-Dihydro-2*H*-pyran, pyridinium *p*-toluenesulfonate (PPTS); (b) $LiAlH_4$; (c) NaH, dimethyl sulfoxide (DMSO), CH_3I; (d) 1,2-ethanediol, PPTS; (e) 4-(dimethylamino)pyridine, $POCl_3$; (f) potassium *tert*-butoxide, DMSO; (g) H_2, Pd/C; (h) pyridinium hydrobromide perbromide.

Scheme II[a]



[a] (a) Potassium *tert*-butoxide, DMSO; (b) $HClO_4$, diethyl ether; (c) *p*-toluenesulfonic acid (*p*-TsOH); (d) 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), *p*-TsOH; (e) $LiAlH_4$; (f) methyllithium; (g) iodine, benzene.

at C-4 was protected as a methyl ether, THP ether at C-1 was deprotected by treatment with pyridinium *p*-toluenesulfonate (PPTS)[14] in 1,2-ethanediol to yield alcohol **14**. When ethanol was used as solvent, the ketal group at C-6 also was completely hydrolyzed. Thus, the use of PPTS and 1,2-ethanediol provides an efficient method for selective deprotection of a THP ether in the presence of an ethylene ketal group.

When alcohol **14** was treated with phosphorous oxychloride and 4-(dimethylamino)pyridine in carbon tetrachloride, dehydration proceeded very fast at room temperature to afford olefin **16** as a major product. Although the reaction yielded chloride **15** as a minor product, it was easily converted to olefin **16** by treatment with potassium *tert*-butoxide in dimethyl sulfoxide (DMSO), and the total yield of olefin **16** from alcohol **14** was 80%. Catalytic hydrogenation of **16** afforded compound **17**. Bromination of **17** with pyridinium hydrobromide perbromide (PHPB) occurred instantly and regioselectively at C-7 to yield bromide **18**.

The position and relative stereochemistry of the bromine and methoxyl groups were assigned on the basis of the ^{1}H NMR coupling constants. The proton signal for the tertiary carbon bearing bromine appears as a doublet of doublets (J = 12.6 and 4.9 Hz) at 4.43 ppm, thus eliminating the possibility of bromine substitution at C-5. The large coupling constant of 12.6 Hz indicates a trans diaxial relationship between 7-H and 8-H protons, leading to the 7α configuration of the bromine atom. The relative stereochemistry of the methoxyl group was also assigned to be 4β by decoupling experiments. The large and similar values of the vicinal coupling constants between the 4-H and two 5-H protons (J = 8.3 and 8.4 Hz) indicate dihedral angles of about 25° and 145°, respectively. Furthermore, the coupling constant between 3a-H and 4-H protons (J = 4.6 Hz) leads to a dihedral angle of about 60°. These geometries are inconsistent with the 4α-methoxyl configuration. The present assignments were confirmed by the X-ray studies of a similar compound (+)**10**.

Dehydrobromination of **18** with potassium *tert*-butoxide in DMSO gave olefin **19** (Scheme II). Deprotection of acetal group of **19**, followed by elimination of methanol with *p*-toluenesulfonic acid (*p*-TsOH), yielded dienone **21**. Dehydrogenation of **21** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in the presence of *p*-TsOH afforded trienone **22**. Reduction of **22** with $LiAlH_4$ at −55 °C gave allylic alcohol **23**, which was extremely unstable and therefore immediately subjected to the next dehydration reaction. The crude product (**23**) was treated with iodine in refluxing benzene, affording the desired 1,8a-dihydroazulene (8a*S*)-(+)-**6** in good yield.

Trienone **22** was methylated with methyllithium at −60 °C to give alcohol **24**, the ^{1}H NMR spectrum of which indicated that the product was a mixture of two steroisomers. Alcohol **24** was similarly dehydrated with iodine in boiling benzene, yielding 1,8a-dihydroazulene (8a*S*)-(+)-**7**. Although tetraenes **6** and **7**, oils with aroma, were relatively unstable, they could be distilled in vacuo and stored in a freezer as dilute hexane solutions.

CD and UV Spectra of Chiral 1,8a-Dihydroazulenes (8a*S*)-(+)-6 and (8a*S*)-(+)-7. The CD spectra of the previous model compounds (1*S*,8a*S*)-(+)-**4** and (1*S*,8a*S*)-(+)-**5** resembled that of the natural product (+)-**1**. However, the CD intensities of the model compounds were about half of that of the natural product. The differnces are presumably due to the extra chirality caused by the methoxyl group at C-1.[6] This interpretation is now supported by the CD data of the present model compound **6**, which lacks the unnecessary methoxyl group.

The CD and UV spectra of (8a*S*)-(+)-**6** are illustrated in Figure 3; the UV spectrum exhibits a $\pi \rightarrow \pi^*$ absorption band of medium intensity at 325.3 nm (ϵ 5200) and an intense band at 225.5 nm (ϵ 24400), which resemble those of natural 1,8a-dihydroazulene (8a*S*)-(+)-**1** (Table I). The CD spectrum shows a positive Cotton effect at 319.2 nm ($\Delta\epsilon$ +8.0) and an intense negative one at 226.8 nm ($\Delta\epsilon$ −37.0). The CD curve of the synthetic model compound **6** is thus quite similar, in the sign, shape, and position of Cotton effects, to that of **1** (Table I). Moreover, the CD intensities of **6** are much stronger and closer to those of the natural product than the former model compounds **4** and **5**. Therefore, 1,8a-dihydroazulene **6** is a better model compound for **1**.

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Table I. UV and CD Spectral and Optical Rotation Data of 1,8a-Dihydroazulene Derivatives

compd	UV λ_{max}, nm	UV ϵ	CD λ_{ext}, nm	CD $\Delta\epsilon$	solvent	$[\alpha]_D$ (hexane)
natural product[a] (8aS)-(+)-1	308.5 227.5	5400 25600	314.0 235.2	+19.7 -47.4	hexane	+1200° (c 0.0554)
model for calcn[a] (8aR)-3	313 219	9900 27300	313 219	-13.9 +46.2	-	-
synthetic (8aS)-(+)-6	325.3 225.5	5200 24400	319.2 226.8	+8.0 -37.0	ethanol	+345° (19 °C) (c 0.100)
synthetic (8aS)-(+)-7	324.2 227.6	6700 26900	308.2 243.0 227.7	+3.5 +5.6 -31.2	ethanol	+323° (19 °C) (c 0.258)
synthetic (1S,8aS)-(+)-4[a]	324.3 223.2	6000 23700	321.0 221.3	+5.7 -24.5	ethanol	+393° (c 0.118)
synthetic (1S,8aS)-(+)-5[a]	324.5 226.2	7200 24300	318.6 240.2 220.7	+4.3 +1.6 -18.1	ethanol	+323° (c 0.207)

[a] Taken from ref 6.

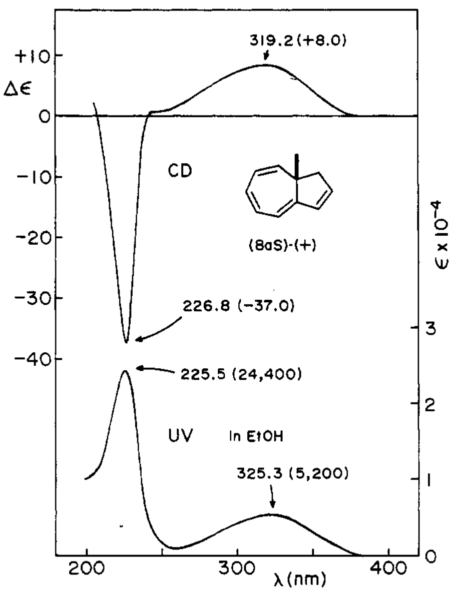

Figure 3. CD and UV spectra of (8aS)-(+)-1,8a-dihydro-8a-methylazulene **6** in ethanol.

As discussed in the previous report,[6] the theoretical calculation of the CD spectra of the model compound (8aR)-**3** gave intense Cotton effects, λ_{ext} 313 nm ($\Delta\epsilon$ -13.9) and λ_{ext} 219 nm ($\Delta\epsilon$ +46.2) (Table I). Since the absolute values of the observed $\Delta\epsilon$'s of the new model compound (8aS)-(+)-**6** are comparable to these theoretical values, the present data experimentally confirms the previous theoretical calculations.

The other model compound (8aS)-(+)-**7** also exhibits similar CD and UV spectra as listed in Table I. Although the negative CD Cotton effect at 227.7 nm is a little weaker than that of **6**, it is stronger than those of the previous model compounds **4** and **5**. Evidently, the methoxyl group at C-1 position diminishes the CD intensity of 1,8a-dihydroazulene system. Substitution of a methyl group at C-6 also diminishes the CD intensity. However, its effect on the CD intensity is weaker than that of the C-1 methoxyl group.

Experimental Section

General Procedures. Melting points are uncorrected. Optical rotations $[\alpha]_D$ were measured on a JASCO DIP-4S spectropolarimeter. UV and CD spectra were recorded on JASCO UVDEC-505 and JASCO J-400X spectrometers, respectively. The purity of all title compounds was shown to be ≥95% by ^{1}H NMR, TLC, HPLC, and/or elemental analyses.

(1*S*,3a*ξ*,8a*S*)-2,3,3a,7,8,8a-Hexahydro-1-hydroxy-8a-methyl-4,6(1*H*,5*H*)-azulenedione 6-Ethylene Acetal (9). The preparation of optically active ketone (1S,3aξ,8aS)-**9** from (8aS)-(+)-3,4,8,8a-tetrahydro-8a-methyl-1,6(2*H*,7*H*)-naphthalenedione (**8**) [mp 50.5–51.0 °C; $[\alpha]_D$ +98.5° (*c* 1.0, benzene)] was previously reported by us.[6] The obtained product **9** is a mixture of the major trans 1S,3aR,8aS isomer **9a** and the minor cis 1S,3aS,8aS isomer **9b**.[13]

X-ray Crystallographic Absolute Stereostructure Determination of (1*S*,3a*R*,4*S*,7*R*,8a*S*)-(+)-7-Bromo-2,3,3a,4,5,7,8,8a-octahydro-1,4-dimethoxy-8a-methyl-6(1*H*)-azulenone 6-Ethylene Acetal (10). Colorless single crystals suitable for the collection of X-ray diffraction data were obtained by recrystallization of bromide **10** from diethyl ether: mp 102 °C; $[\alpha]_D$ +49.6° (*c* 1.003, $CHCl_3$); high-resolution mass spectrum (CI with 2-methylpropane), calcd for $C_{15}H_{25}{}^{81}BrO_4$ + H 351.09952, found 351.09489; calcd for $C_{15}H_{25}{}^{79}BrO_4$ + H 349.10149, found 349.10125. Anal. Calcd for $C_{15}H_{25}O_4Br$: C, 51.58; H, 7.22; Br, 22.88. Found: C, 51.64; H, 7.16; Br, 22.97.

A crystal (dimensions 0.33 × 0.40 × 0.43 mm) was selected for data collection and mounted on a Rigaku AFC-5 automated four circle diffractometer. The crystal was found to be orthorhombic, and unit cell parameters and the orientation matrix were obtained. Data collection was carried out by using a $2\theta - \theta$ scan: formula, $C_{30}H_{50}Br_2O_8$; formula weight, 698.50; space group, $P2_12_12_1$; a = 15.139 (3) Å, b = 22.597 (4) Å, c = 9.268 (1) Å; vol = 3176.8 (9) Å^3; Z = 4; ρ(obsd) = 1.443 g/cm^3; ρ(calcd) = 1.452 g/cm^3; diffractometer, Rigaku AFC-5; radiation, Mo Kα (0.71073 Å); monochrometer, graphite crystal; linear abs coeff, 25.557 cm^{-1}; temp, 24 °C; scan type, $2\theta - \theta$; scan speed, 3.0 deg/min; scan range, 1.2° + 0.5° tan θ; 2θ scan limits, 2.0°–50.0°; std reflections, 3 per 50 reflections; indices, (5,1,0), (0,6,0), (2,0,2); cryst stability, no indication of std reflection decay during data collection; total reflections scanned, 3304; unique data $F_o^2 > 2.5\sigma(F_o^2)$, 1387. These data indicate that the two crystallographically independent molecules of bromide **10** are contained in one asymmetric unit.

At first, the positions of the two bromine atoms were found by the direct method, and then those of the remaining non-hydrogen atoms were found by the successive Fourier synthesis. Absorption correction was made by using the data of face indices and the size of the crystal. All hydrogen atoms were placed in idealized positions. Block diagonal least-squares refinement of positional parameters, anisotropic thermal parameters for non-hydrogen atoms, and isotropic thermal parameters for hydrogen atoms, including anomalous scattering factors of bromine, oxygen, and carbon atoms, led to the final convergence with R = 0.0427 (final no. of variables, 561) for the 1S,3aR,4S,7R,8aS absolute configuration, while a similar calculation for the mirror image structure gave R = 0.0485. So, the absolute stereochemistry of (+)-**10** was determined to be 1S,3aR,4S,7R,8aS as illustrated in Figure 2.

(1*S*,3a*R*,8a*S*)-2,3,3a,7,8,8a-Hexahydro-8a-methyl-1-(3,4,5,6-tetrahydro-2*H*-pyran-2-yloxy)-4,6(1*H*,5*H*)-azulenedione 6-Ethylene Acetal (11a) and Its 1*S*,3a*S*,8a*S*

Stereoisomer (11b). To a solution of alcohol (1*S*,3a*ξ*,8a*S*)-**9** (10 g, 41.6 mmol) in dry dichloromethane (300 mL) were added 3,4-dihydro-2*H*-pyran (4.5 mL, 4.2 g, 49.9 mmol) and pyridinium *p*-toluenesulfonate (0.345 g, 1.3 mmol). After being stirred under nitrogen at room temperature for 24 h, the reaction mixture was poured into dilute aqueous $NaHCO_3$ solution and extracted with dichloromethane. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was chromatographed on silica gel (hexane/EtOAc, 4:1), giving the major product of 3,4,5,6-tetrahydro-2*H*-pyran-2-yl (THP) ether, *trans*-(1*S*,3a*R*,8a*S*)-**11a**, (9.96 g, 74%) as a syrup: IR ($CHCl_3$) ν_{max} 2930, 2860, 1690, 1465, 1450, 1350, 1135, 1110, 1075, 1030 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 0.75 (3 H, s, 8a-CH_3), 1.2–2.6 (14 H, m), 2.67 (2 H, s, 5-H), 3.07 and 3.12 (total 1 H, t, *J* = 8.8 Hz, 3a-H), 3.16–4.00 (3 H, m), 3.94 (4 H, br s, acetal), 4.63 (1 H, br s, $W_{1/2}$ = 6 Hz); MS (CI with 2-methylpropane) *m/z* 325 (M + H, relative intensity 14), 269 (21), 241 (100), 223 (48), 197 (22), 181 (27), 179 (27); high-resolution mass spectrum, calcd for $C_{18}H_{28}O_5$ + H 325.20148, found 325.20165.

From the more polar fractions, the minor product of the other stereoisomer, *cis*-(1*S*,3a*S*,8a*S*)-**11b**, (1.96 g, 15%) was obtained as a syrup: IR ($CHCl_3$) ν_{max} 2950, 2880, 1705, 1470, 1460, 1440, 1360, 1140, 1130, 1100, 1080, 1035 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.19 and 1.22 (total 3 H, s, 8a-CH_3) 1.34–2.32 (14 H, m), 2.45 (1 H, d, *J* = 12.0 Hz, 5-H), 2.84 (1 H, m, 3a-H), 2.90 (1 H, d, *J* = 12.0 Hz, 5-H), 3.3–4.1 (3 H, m), 3.96 (4 H, s, acetal), 4.32 and 4.61 (total 1 H, br s); MS (CI with 2-methylpropane) *m/z* 325 (M + H, 3) 281 (4), 241 (100), 223 (20), 197 (37), 179 (86), 151 (57); high-resolution mass spectrum, calcd for $C_{18}H_{28}O_5$ + H 325.20148, found 325.20224.

(1*S*,3a*R*,4*S*,8a*S*)-2,3,3a,4,5,7,8,8a-Octahydro-4-hydroxy-8a-methyl-1-(3,4,5,6-tetrahydro-2*H*-pyran-2-yloxy)-6(1*H*)-azulenone 6-Ethylene Acetal (12). To a suspension of $LiAlH_4$ (1.7 g, 29.8 mmol) in dry diethyl ether (30 mL) cooled at 0 °C was added dropwise a solution of ketone *trans*-(1*S*,3a*R*,8a*S*)-**11a** (9.668 g, 29.8 mmol) in dry diethyl ether (70 mL) and dry tetrahydrofuran (THF, 12 mL). After being stirred at room temperature for 1.5 h, the reaction mixture was quenched with wet diethyl ether and ethyl acetate and then treated with a minimum amount of water to precipitate hydroxides. The organic layer was evaporated to dryness, affording alcohol **12** (9.51 g, 98%) as a syrup: IR ($CHCl_3$) ν_{max} 3620, 3470, 2980, 2880, 1680, 1470, 1460, 1440, 1360, 1140, 1130, 1080 1065, 1035 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.99 (3 H, s, 8a-CH_3), 1.1–2.9 (18 H, m), 3.2–4.2 (4 H, m), 3.93 (4 H, s, acetal), 4.65 (1 H, m).

(1*S*,3a*R*,4*S*,8a*S*)-2,3,3a,4,5,7,8,8a-Octahydro-4-methoxy-8a-methyl-1-(3,4,5,6-tetrahydro-2*H*-pyran-2-yloxy)-6-(1*H*)-azulenone 6-Ethylene Acetal (13). A mixture of sodium hydride (1.24 g, 51.7 mmol) and dry dimethyl sulfoxide (DMSO, 30 mL) was stirred at 50 °C for 2.5 h. After the mixture was cooled to room temperature, a solution of alcohol **12** (8.43 g, 25.8 mmol) in dry tetrahydrofuran (20 mL) and dry dimethyl sulfoxide (32.5 mL) was added dropwise, and the mixture was stirred at 35 °C for 2.5 h. After iodomethane (6.4 mL, 14.6 g, 103 mmol) was added under ice cooling, the reaction mixture was stirred at room temperature for 1.8 h, evaporated in vacuo to remove excess iodomethane, poured into ice–water, and extracted with ethyl acetate. The organic layer was washed with water and then with brine, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was chromatographed on silica gel (hexane/EtOAc, 5:1) to yield methyl ether **13** (8.05 g, 92%) as a syrup: IR ($CHCl_3$) ν_{max} 2940, 2870, 1730, 1455, 1355, 1325, 1130, 1080, 1025 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.72 (3 H, s, 8a-CH_3), 1.15–2.8 (17 H, m), 3.30 (3 H, s, OCH_3), 3.3–4.2 (4 H, m), 3.93 (4 H, s, acetal), 4.62 and 4.65 (total 1 H, br s).

(1*S*,3a*R*,4*S*,8a*S*)-2,3,3a,4,5,7,8,8a-Octahydro-1-hydroxy-4-methoxy-8a-methyl-6(1*H*)-azulenone Ethylene Acetal (14). A mixture of THP ether **13** (8.5 g, 25.0 mmol), dry dichloromethane (500 mL), and 1,2-ethanediol (14 mL, 15.5 g, 250 mmol) was refluxed under nitrogen for 1 h, during which time a trace amount of water was removed with a water-separating apparatus containing dried molecular sieves 4A. After pyridinium *p*-toluenesulfonate (0.677 g, 2.5 mmol) was added, the reaction mixture was refluxed for 12 h, cooled to room temperature, and poured into an aqueous sodium bicarbonate solution. The separated organic layer was washed with water and then with brine, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was chromatographed on silica gel (hexane/EtOAc, 1:1) to give alcohol **14** (4.97 g, 78%) as colorless fine needles: mp 99–100 °C; IR ($CHCl_3$) ν_{max} 3600, 3460, 2940, 2880, 2830, 1465, 1450, 1370, 1240, 1120, 1090, 1060 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.86 (3 H, s, 8a-CH_3), 1.0–2.9 (12 H, m), 3.29 (3 H, s, OCH_3), 3.3–3.8 (2 H, m) 3.92 (4 H, s, acetal); MS (CI with 2-methylpropane) *m/z* 257 (M + H, 17), 225 (100), 207 (99), 181 (56), 163 (40), 129 (96); high-resolution mass spectrum, calcd for $C_{14}H_{24}O_4$ + H 257.17527, found 257.17563.

As a byproduct, (1*S*,3a*R*,4*S*,8a*S*)-2,3,3a,4,5,7,8,8a-octahydro-1-hydroxy-4-methoxy-8a-methyl-6(1*H*)azulenone (**25**) (0.6 g) was obtained: colorless needles, mp 116–118 °C; ^1H NMR (60 MHz, $CDCl_3$) δ 0.80 (3 H, s, 8a-CH_3), 1.0–2.3 (8 H, m), 2.3–3.2 (4 H, m), 3.35 (3 H, s, OCH_3), 3.4–4.0 (2 H, m); MS (CI with 2-methylpropane) *m/z* 213 (M + H, 36), 195 (34), 181 (100), 163 (100); high-resolution mass spectrum, calcd for $C_{12}H_{20}O_3$ + H 213.14906, found 213.14807.

(3a*R*,8a*S*)-3a,4,5,7,8,8a-Hexahydro-4-methoxy-8a-methyl-6(3*H*)-azulenone 6-Ethylene Acetal (16) and (1*ξ*,3a*R*,8a*S*)-1-Chloro-2,3,3a,4,5,7,8,8a-octahydro-4-methoxy-8a-methyl-6(1*H*)-azulenone 6-Ethylene Acetal (15). To a solution of 4-(dimethylamino)pyridine (18.6 g, 152 mmol) in carbon tetrachloride (400 mL) was added a solution of alcohol **14** (2.71 g, 10.6 mmol) in carbon tetrachloride (140 mL). To the mixture was added phosphorous oxychloride (1.95 mL, 3.24 g, 21.1 mmol) all at once at room temperature under nitrogen. The reaction mixture was stirred at room temperature for 1.8 h and poured into an aqueous $NaHCO_3$ solution. The organic layer was washed with water and then with brine, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue containing 4-(dimethylamino)pyridine was subjected to a short column chromatography on silica gel, giving a crude product (2.507 g). The crude product was further purified by a high-performance liquid chromatography (HPLC) on silica gel (hexane/EtOAc, 3:1), affording olefin **16** (1.40 g, 55%) as a major product: IR ($CHCl_3$) ν_{max} 2920, 2820, 1615, 1460, 1355, 1320, 1255, 1170, 1130, 1080, 1060, 995, 950 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.01 (3 H, s, 8a-CH_3), 1.39–2.85 (9 H, m), 3.28 (3 H, s, OCH_3), 3.53 (1 H, ddd, *J* = 8.3, 8.3, 4.5 Hz, 4-H), 3.91 (4 H, s, acetal), 5.38 (1 H, br d, *J* = 5.7 Hz, 1-H), 5.62 (1 H, ddd, *J* = 5.7, 2.6, 1.4 Hz, 2-H).

From the more polar fractions, chloride **15** (0.83 g, 29%) was obtained: IR (neat) ν_{max} 2960, 2940, 2880, 2820, 1465, 1455, 1370, 1350, 1330, 1245, 1170, 1120, 1090, 1060 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.04 (3 H, s, 8a-CH_3), 1.1–2.8 (m), 3.29 (3 H, s, OCH_3), 3.54 (1 H, m), 3.93 (4 H, s, acetal); MS (CI with 2-methylpropane) *m/z* 277 (M + H, 7), 275 (M + H, 22), 245 (43), 243 (100), 207 (100), 201 (22), 199 (62), 181 (48), 163 (56), 145 (18), 129 (81), 99 (70); high-resolution mass spectrum, calcd for $C_{14}H_{23}{}^{37}ClO_3$ + H 277.13844; found 277.13919; calcd for $C_{14}H_{23}{}^{35}ClO_3$ + H 275.14139, found 275.14170.

(3a*R*,8a*S*)-3a,4,5,7,8,8a-Hexahydro-4-methoxy-8a-methyl-6(3*H*)-azulenone 6-Ethylene Acetal (16) from Chloride 15. To a solution of chloride **15** (0.100 g, 0.36 mmol) in dimethyl sulfoxide (5 mL) was added potassium *tert*-butoxide (0.163 g, 1.46 mmol) under nitrogen. After being stirred at room temperature for 14 h, the reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with water and then with brine, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was subjected to a short column chromatography on silica gel, yielding olefin **16** (0.076 g, 88%) as a syrup.

(3a*R*,4*S*,8a*S*)-(+)-2,3,3a,4,5,7,8,8a-Octahydro-4-methoxy-8a-methyl-6(1*H*)-azulenone 6-Ethylene Acetal (17). A mixture of olefin **16** (1.895 g, 7.96 mmol), 5% palladium on charcoal (0.170 g), and dry ethanol (180 mL) was stirred under hydrogen at room temperature for 2.4 h. The reaction mixture was subjected to a short column chromatography on silica gel to remove the catalyst. The crude product was further purified by an HPLC on silica gel giving compound 17 (1.895 g, 99%) as a syrup: IR ($CHCl_3$) ν_{max} 2960, 2920, 1460, 1445, 1360, 1115, 1085, 1055 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 0.96 (3 H, s, 8a-CH_3), 1.1–2.3 (12 H, m), 2.51 (1 H, ddd, *J* = 14.2, 8.5, 1.9 Hz, 5-H), 3.30 (3 H, s, OCH_3), 3.50 (1 H, ddd, *J* = 8.5, 8.0, 4.1 Hz, 4-H), 3.94 (4 H, s, acetal); $[\alpha]^{20}_D$ +41.5° (*c* 0.347, $CHCl_3$). Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 70.12; H, 9.94.

(3a*R*,4*S*,7*R*,8a*S*)-(+)-7-Bromo-2,3,3a,4,5,7,8,8a-octahydro-4-methoxy-8a-methyl-6(1*H*)-azulenone 6-Ethylene Acetal (18). To a solution of acetal **17** (3.94 g, 16.4 mmol) in dry tetrahydrofuran (70 mL) was added pyridinium hydrobromide perbromide (5.24 g, 18.0 mmol) all at once. After being stirred for 2.5 min under nitrogen, the reaction mixture was immediately poured into an aqueous $NaHCO_3$ solution and extracted with ethyl acetate. The organic layer was washed with water, aqueous $CuSO_4$, water, and brine and evaporated to dryness. The residue was subjected to a short column chromatography on silica gel (hexane/EtOAc, 2:1), giving bromide **18** (4.82 g, 92%) as white crystals. The product was further purified by recrystallization from diethyl ether: mp 93 °C dec; IR ($CHCl_3$) ν_{max} 2950, 2880, 1460, 1335, 1170, 1085, 1050 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 0.96 (3 H, s, 8a-CH_3), 1.2–2.2 (9 H, m), 1.86 (1 H, dd, J = 15.3, 8.3 Hz, 5-H), 2.36 (1 H, dd, J = 13.7, 4.9 Hz, 8-H), 2.65 (1 H, dd, J = 15.3, 8.4 Hz, 5-H), 3.24 (3 H, s, OCH_3), 3.40 (1 H, ddd, J = 8.4, 8.3, 4.6 Hz, 4-H), 3.8–4.2 (4 H, m, acetal), 4.43 (1 H, dd, J = 12.6, 4.9 Hz, 7-H) [^{1}H NMR decoupling experiments: irradiation at 2.36 ppm changed the signal at 4.43 ppm (dd → d, J = 12.6 Hz); irradiation at 4.43 ppm changed the signal at 2.36 ppm (dd → d, J = 13.7 Hz); irradiation at 3.40 ppm changed the signals at 2.65 ppm (dd → d, J = 15.3 Hz) and 1.86 ppm (dd → d, J = 15.3 Hz)]; $[\alpha]^{19}_D$ +22.8° (*c* 1.001, $CHCl_3$); MS (CI with 2-methylpropane) *m/z* 321 (M + H, 2), 319 (M + H, 3), 289 (56), 287 (58), 249 (28), 208 (30), 207 (100), 129 (100), 125 (43), 99 (33); high-resolution mass spectrum, calcd for $C_{14}H_{23}{}^{81}BrO_3$ + H 321.08895, found 321.09305; calcd for $C_{14}H_{23}{}^{79}BrO_3$ + H 319.09092, found 319.09068.

(3a*R*,4*S*,8a*S*)-(−)-2,3,3a,4,5,8a-Hexahydro-4-methoxy-8a-methyl-6(1*H*)-azulenone 6-Ethylene Acetal (19). To a solution of bromide **18** (4.80 g, 15.0 mmol) in dry dimethyl sulfoxide (140 mL) heated at 35 °C, was added potassium *tert*-butoxide (6.46 g, 57.2 mmol). The reaction mixture was stirred at 50 °C for 3.7 h under nitrogen, poured into ice–water, and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was subjected to a column chromatography on silica gel (hexane/EtOAc, 7:1), giving olefin **19** (2.67 g, 75%) as a syrup: IR ($CHCl_3$) ν_{max} 2950, 2880, 2820, 1655, 1450, 1370, 1350, 1320, 1170, 1140, 1115, 1085, 1050, 1020, 980, 950 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.03 (3 H, s, 8a-CH_3), 1.4–2.7 (9 H, m), 3.28 (3 H, s, OCH_3), 3.59 (1 H, m, 4-H), 3.94 (4 H, br s, acetal), 5.39 (1 H, dd, J = 11.7, 1.8 Hz, 7-H), 5.80 (1 H, d, J = 11.7 Hz, 8-H); $[\alpha]^{19}_D$ −72.8° (*c* 1.185, $CHCl_3$).

(3a*R*,4*S*,8a*S*)-2,3,3a,4,5,8a-Hexahydro-4-methoxy-8a-methyl-6(1*H*)-azulenone (20). To a solution of acetal **19** (2.654 g, 11.1 mmol) in diethyl ether (100 mL) was added diethyl ether (20 mL) saturated with aqueous 70% $HClO_4$. The reaction mixture was stirred under nitrogen at room temperature for 2.5 h, poured into aqueous $NaHCO_3$, and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated in vacuo, giving enone **20** (1.924 g, 89%) as a syrup: IR ($CHCl_3$) ν_{max} 2950, 2920, 2860, 1660, 1640, 1600, 1460, 1480, 1115, 1080, 1060 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.18 (3 H, s, 8a-CH_3), 1.4–2.5 (7 H, m), 2.8–3.2 (2 H, m, 5-H), 3.31 (3 H, s, OCH_3), 3.73 (1 H, m, 4-H), 5.84 (1 H, d, J = 10.6 Hz, 7-H), 6.55 (1 H, d, J = 10.6 Hz, 8-H).

(3a*R*,8a*S*)-2,3,3a,8a-Tetrahydro-8a-methyl-6(1*H*)-azulenone (21). A mixture of enone **20** (1.881 g, 9.7 mmol), dry benzene (200 mL), and *p*-toluenesulfonic acid (0.167 g, 0.97 mmol) was stirred at 40 °C for 6.5 h. After being cooled to room temperature, the mixture was subjected to a short column chromatography on silica gel. The obtained crude product (1.2 g) was purified by an HPLC on silica gel (hexane/EtOAc, 4:1), giving dienone **21** (1.038 g, 66%) as a syrup: IR ($CHCl_3$) ν_{max} 2950, 2860, 1645, 1605, 1460, 1445, 1400 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.00 (3 H, s, 8a-CH_3), 1.38–2.48 (6 H, m), 2.94 (1 H, m, 3a-H), 5.90 (1 H, dd, J = 11.5, 1.8 Hz, 7-H), 6.05 (1 H, ddd, J = 11.3, 1.8, 1.3 Hz, 5-H), 6.39 (1 H, dd, J = 11.3, 3.1 Hz, 4-H), 6.61 (1 H, d, J = 11.5 Hz, 8-H); MS (EI) *m/z* (parent, 28), 147 (53), 134 (58), 119 (70), 107 (40), 106 (38), 105 (43), 91 (100); high-resolution mass spectrum, calcd for $C_{11}H_{14}O$ 162.10446, found 162.10449.

(8a*S*)-1,8a-Dihydro-8a-methyl-6(2*H*)-azulenone (22). A mixture of dienone **21** (0.500 g, 3.1 mmol), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 98%, 1.428 g, 6.2 mmol), *p*-toluenesulfonic acid (0.103 g, 0.59 mmol), and dry benzene (120 mL) was stirred at 50 °C for 24 h. After being cooled to room temperature, the reaction mixture was subjected to a short column chromatography on silica gel. The crude product was further purified by a preparative thin-layer chromatography (TLC) on silica gel and by an HPLC on silica gel (hexane/EtOAc, 5:1), affording trienone **22** (0.236 g, 48%): IR ($CHCl_3$) ν_{max} 2980, 2950, 2850, 1640, 1620, 1600, 1570, 1445, 1405, 1285 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.22 (3 H, s, 8a-CH_3), 1.99–2.41 (2 H, m, 1-H), 2.23–2.55 (2 H, m, 2-H), 5.83–6.06 (3 H, m), 6.33 (1 H, d, J = 11.6 Hz), 6.84 (1 H, d, J = 11.4 Hz). The starting material of dienone **21** (0.073 g) was recovered.

(6ξ,8a*S*)-1,2,6,8a-Tetrahydro-8a-methyl-6-azulenol (23). To a suspension of $LiAlH_4$ (0.075 g, 2.0 mmol) in dry diethyl ether (1 mL) cooled at −55 °C was added dropwise a solution of trienone **22** (0.106 g, 0.67 mmol) in dry diethyl ether (2.5 mL) under nitrogen. The reaction mixture was stirred at −55 °C for 1.5 h, quenched with wet diethyl ether, and treated with a minimum amount of water to precipitate hydroxides. The organic layer was evaporated in vacuo, affording alcohol **23** (0.099 g, 92%) as an oil: ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.16 (3 H, s, 8a-CH_3), 1.6–2.7 (4 H, m), 5.06–6.36 (6 H, m). Since the allylic alcohol **23** was extremely unstable, the product was immediately subjected to the next reaction.

(8a*S*)-(+)-1,8a-Dihydro-8a-methylazulene (6). To a solution of alcohol **23** (0.099 g) in dry benzene (20 mL) was added a solution of iodine (0.005 g) in dry benzene (5 mL), and the mixture was vigorously refluxed for 1 h in an oil bath heated at 110 °C. After being cooled to room temperature, the reaction mixture was subjected to a short column chromatography on silica gel (hexane). The product was further purified by an HPLC on silica gel (hexane) and then distilled in vacuo with a short-path distillation apparatus giving dihydroazulene **6** (0.030 g, 34%) as an oil with aroma: bp 40–60 °C (0.5–0.9 kPa); ^{1}H NMR (100 MHz, $CDCl_3$) δ 0.78 (3 H, s, 8a-CH_3), 2.72 (2 H, br s, 1-H), 5.54 (1 H, d, J = 9.0 Hz), 5.87–6.49 (6 H, m); MS (EI, 70 eV) *m/z* 144 (parent, 100), 130 (100), 129 (100), 115 (68), 77 (48), 64 (68), 51 (68); high-resolution mass spectrum, calcd for $C_{11}H_{12}$ 144.0938, found 144.0932.

(6ξ,8a*S*)-1,2,6,8a-Tetrahydro-6,8a-dimethyl-6-azulenol (24). To a solution of trienone **22** (0.096 g, 0.60 mmol) in dry diethyl ether (15 mL) cooled at −60 °C was added dropwise a solution of methyllithium in diethyl ether (1 M, 1.2 mL, 1.2 mmol). After being stirred at −60 °C for 2.4 h, the reaction mixture was poured into ice–water and extracted with diethyl ether. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated in vacuo giving alcohol **24** (0.109 g, 100%) as an oil: ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.14 and 1.20 (total 3 H, s, 8a-CH_3), 1.30 and 1.44 (total 3 H, s, 6-CH_3), 1.7–2.1 (2 H, m, 1-H), 2.1–2.6 (2 H, m, 2-H), 5.2–5.8 (5 H, m), 6.14 (1 H, d, J = 12.4 Hz). The ^{1}H NMR spectrum indicates that the product is a mixture of two stereoisomers.

(8a*S*)-(+)-1,8a-Dihydro-6,8a-dimethylazulene (7). To a solution of alcohol **24** (0.109 g, 0.6 mmol) in dry benzene (20 mL) was added a solution of iodine (0.003 g, 0.012 mmol) in dry benzene (3 mL). The reaction mixture was refluxed for 40 min in an oil bath heated at 110 °C. After being cooled to room temperature, the mixture was chromatographed on silica gel (hexane). The crude product obtained was further purified by an HPLC on silica gel (hexane), yielding dihydroazulene **7** (0.061 g, 64%) as an oil with aroma. The analytical sample was obtained by the distillation in vacuo using a short-path distillation apparatus: bp 40–52 °C (0.3–0.1 kPa); ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.76 (3 H, s, 8a-CH_3), 2.01 (3 H, s, 6-CH_3), 2.71 (2 H, br s, 1-H), 5.54 (1 H, d, J = 10.6 Hz), 5.8–6.4 (5 H, m); MS (EI, 70 eV) *m/z* 158 (parent, 100), 144 (73), 143 (100), 129 (65), 128 (100), 115 (100), 77 (50), 71 (57), 51 (42); high-resolution mass spectrum, calcd for $C_{12}H_{14}$ 158.1096, found 158.1100.

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Registry No. (8a*S*)-(+)-1, 85337-23-1; (8a*S*)-(+)-6, 102934-57-6; (8a*S*)-(+)-7, 119326-97-5; **9a**, 94198-87-5; **9b**, 94198-84-2; (+)-**10**, 119365-57-0; **11a**, 119326-98-6; **11b**, 119365-59-2; **12**, 119326-99-7; **13**, 119327-00-3; **14**, 119327-01-4; **14** (ketone), 119327-12-7; (1*R*)-**15**, 119365-58-1; (1*S*)-**15**, 119327-02-5; **16**, 119327-03-6; **17**, 119327-04-7; **18**, 119327-05-8; **19**, 119327-06-9; **20**, 119327-07-0; **21**, 119327-08-1; **22**, 119327-09-2; *cis*-**23**, 119327-10-5; *trans*-**23**, 119327-13-8; *cis*-**24**, 119327-11-6; *trans*-**24**, 119327-14-9.

Rate Constants for Halogen Atom Transfer from Representative α-Halocarbonyl Compounds to Primary Alkyl Radicals

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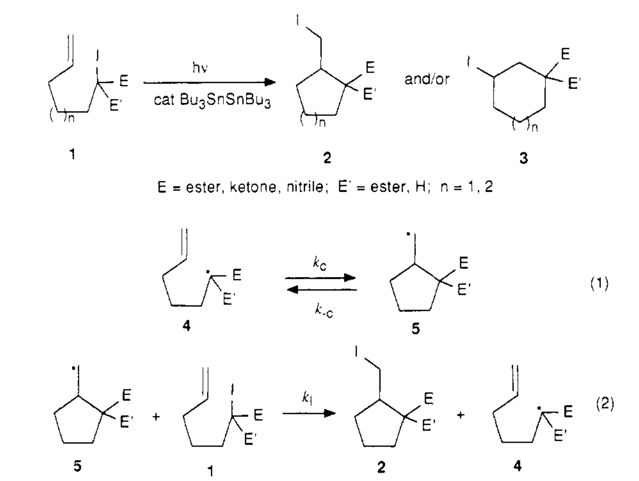
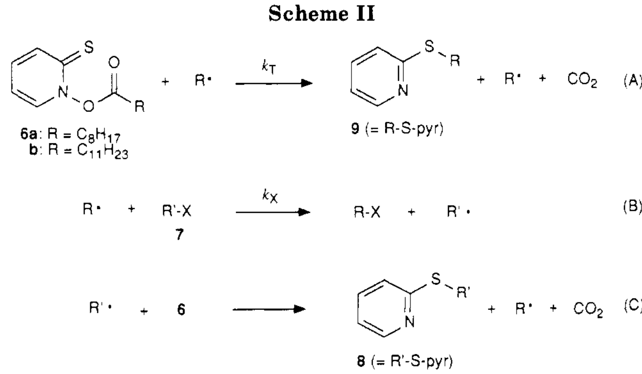
Rate constants for halogen atom transfer from diethyl methyliodomalonate (**7a**), iodoacetonitrile (**7b**), ethyl 2-methyl-2-iodopropanoate (**7c**), ethyl iodoacetate (**7d**), diethyl methylbromomalonate (**7e**), and ethyl bromoacetate (**7f**) to simple primary alkyl radicals have been studied by a variety of competition reactions. The Arrhenius functions for halogen atom transfer to the undecyl radical from halides **7d** and **7f** are log (k_I, M^{-1} s^{-1}) = 10.4 − 4.4/θ and log (k_{Br}, M^{-1} s^{-1}) = 10.4 − 8.2/θ, respectively. The rate constants for halogen atom transfer to a primary radical from the series of compounds **7a–f** at 50 °C are 1.8×10^9, 1.7×10^9, ca. 6×10^8, 2.6×10^7, 1.0×10^6, and 7.0×10^4 M^{-1} s^{-1}, respectively. The kinetic values are useful for the planning of synthetic methods that incorporate an atom transfer–cyclization process.

The cyclization of electrophilic radicals by the atom transfer method is emerging as a mild and powerful method for the formation of rings.[4] A generic example is shown in Scheme I. Irradiation of an α-iodo ester, ketone, malonate, or cyanomalonate (1) provides exo (2) and/or endo (3) cyclized products, depending upon the nature of the groups E and E′, the substituents on the alkene, and the chain length. The propagation steps (Scheme I) for this chain reaction are cyclization (step 1) and atom transfer (step 2). To establish that the products of such reactions were formed under kinetic control, we needed to determine whether or not atom transfer (step 2) was faster than ring opening of the cyclized product. Unfortunately, no absolute rate constants for reactions of the substrates or appropriate models required for an analysis of Scheme I were known, although control experiments with Bu_3SnH served to set upper limits for k_{-c}.[4b] We now report measurements of k_I, the halogen atom transfer step of Scheme I, for some representative α-halo esters, nitriles, and malonates. The results confirm that kinetic cyclization products are formed in the atom transfer cyclization sequence.[4b] Furthermore, the rate constants obtained will be valuable for synthetic planning of halogen atom transfer reactions.

Scheme I



Scheme II



Products from Halogen Atom Transfer Reactions. Rate constants for halogen atom transfer from alkyl halides can be measured by a kinetic adaptation[5] of the Barton thiohydroxamate ester decomposition reactions.[6] As summarized in Scheme II, a radical chain reaction (following initiation by visible-light irradiation) of an alkyl thiohydroxamate ester **6** in the absence of added reagents (step A) gives a decarboxylated alkyl pyridyl sulfide **9** by addition of the alkyl radical (R•) to its own precursor. The rate constant for this self-trapping reaction, k_T, has been measured for the case where R is octyl[7] or undecyl.[8]

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