6-Amino-9-[2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]purine (22).[26] Adenosine (**21**) (0.259 g, 0.972 mmol) and imidazole (0.536 g, 7.89 mmol) were dissolved in dry dimethylformamide (1 mL), followed by *tert*-butyldimethylsilyl chloride (0.638 g, 4.2 mmol). The solution was stirred under N_2 for 2 h until homogeneous and then allowed to sit for 24 h. The solution was pumped to dryness, taken up in ethyl acetate, and eluted through a short silica gel scrubber column with 1:1 hexane/ethyl ether. Final purification by flash chromatography on silica gel (1:1 hexane/ethyl ether) provided 0.444 g (0.728 mmol, 75%) of a white solid: mp 142–144 °C (lit.[26] mp 142–144 °C); ^{1}H NMR ($CDCl_3$) δ −0.04 (s), 0.11 (s), 0.13 (s), 0.80 (s), 0.94 (s), 0.96 (s), 3.72–4.04 (m, 2 H), 4.14 (m, 1 H), 4.37 (m, 1 H), 4.75 (m, 1 H), 5.90 (br s, 1 H), 6.06 (d, 1 H, J = 5.1 Hz), 8.18 (s, 1 H), 8.37 (s, 1 H).

6-Iodo-9-[2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]purine (23). To a solution of 6-amino-9-[2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]purine (**22**) (0.316 g, 0.519 mmol) in dry nitrogen purged hexane (30 mL) was added trimethylsilyl iodide (0.125 mL, 0.880 mmol) followed by diiodomethane (0.90 mL, 11.2 mmol) and *n*-pentyl nitrite (1.50 mL, 11.1 mmol). The mixture was stirred at 60 °C for 24 h under N_2. Upon cooling, hexane (20 mL) was added and the reaction mixture was extracted with saturated sodium sulfite (5 mL) and water (5 mL). The combined aqueous phases were extracted with ethyl ether (60 mL). The combined extracts were dried (Na_2SO_4), and the solvent was removed under reduced pressure. The residue was purified on silica gel plates developed with 1:1 hexane/ethyl ether. The band at R_f 0.80 provided 0.261 g (0.363 mmol, 70%) of **23** as a clear oil: ^{1}H NMR ($CDCl_3$) δ −0.04 (s), 0.10 (s), 0.13 (s), 0.78 (s), 0.93 (s), 0.95 (s), 3.71–4.19 (m, 3 H), 4.31 (t, 1 H, J = 3.8 Hz), 4.63 (t, 1 H, J = 4.6 Hz), 6.08 (d, 1 H, J = 5.1 Hz), 8.48 (s, 1 H), 8.61 (s, 1 H); UV (EtOH) λ_{max} 276 nm (ε 1.1 × 10^4); mass spectrum m/z (relative intensity) (30 eV) 705 (M^+–CH_3, 0.4), 663 (M^+–C_4H_9, 12.6), 417 (2.3), 403 (5.7), 261 (6.7), 231 (4.5), 149 (4.9), 147 (10.5), 133 (3.9). Anal. Calcd for $C_{28}H_{53}N_4IO_4Si_3$: C, 46.65; H, 7.41; N, 7.77. Found: C, 46.30; H, 7.38; M, 7.64.

6-Acetonyl-9-[2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]purine (24). Following procedure B the enolate anion of acetone was photolyzed with 6-iodo-9-[2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]purine (**23**) (0.551 mmol). Purification on silica gel plates using 1:1 hexane/ethyl ether as the developer produced **24**, 0.183 g (0.281 mmol, 51%),[28] R_f 0.53, as a yellow solid: mp 108–110 °C; ^{1}H NMR ($CDCl_3$) δ −0.04 (s), 0.11 (s), 0.14 (s), 0.79 (s), 0.94 (s), 0.96 (s), 2.17 (s), 2.29 (s), 3.72–4.75 (m), 5.81–6.14 (m), 8.22 (s), 8.26 (s), 8.41 (s), 8.89 (s); UV (EtOH) λ_{max} 362 nm (ε 3.0 × 10^4), 345 (2.5 × 10^4), 330 sh (1.8 × 10^4), 264 (3.8 × 10^3); mass spectrum, m/z (relative intensity) (30 eV) 650 (M^+, 0.8), 635 (M^+–CH_3, 4.1), 593 (M^+–C_6H_9, 100), 447 (13.2), 417 (12.5), 343 (18.0), 333 (83.0), 301 (17.7), 285 (18.0), 275 (16.0), 261 (44.1), 231 (35.9), 211 (30.1), 177 (31.0), 147 (66.3), 133 (9.6), 115 (32.5). Anal. Calcd for $C_{31}H_{58}N_4O_5Si_3$: C, 57.19; H, 8.98; N, 8.60. Found: C, 57.09; H, 8.60; N, 8.45.

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Total Synthesis and Absolute Configuration of Zeylena

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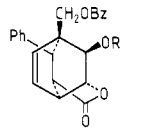
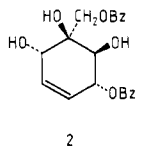
Zeylena (**1a**), isolated from the methanol extract of the roots of *Uvaria zeylanica* (Annonaceae), has been totally synthesized by an intramolecular Diels–Alder reaction of (2*R*)-*trans*-3-[(*E*)-cinnamoyloxy]-2-hyxroxy-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (**3c**). The absolute configuration of **1a** formerly proposed has been established by the present synthesis.

Zeylena (**1a**) and zeylenol (**2**) were isolated from the methanol extract of the roots of *Uvaria zeylanica* L. (Annonaceae) during the extensive work on tumor inhibitory constituents of these species.[1] Although both



1a R = H
1b R = Ac
1c R = COCH=CHPh



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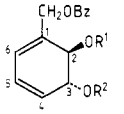
compounds were found to be inactive in the P-338 lymphocytic leukemia test system, their biogenetic relationship[2] to other *Uvaria* constituents has stimulated much interest.[1,3] The structure of **1a** was established by the ^{1}H NMR spectra of **1a** and derivatives, and the absolute configuration has been postulated on the basis of the CD curve of the octahydro ketone derived by a catalytic hydrogenation of **1a**, followed by oxidation.[1]

In continuation of our study of highly oxygenated cyclohexane compounds,[4] we now describe a total synthesis of **1a** starting from (2*R*)-*trans*-2,3-dihydroxy-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene[4] (**3a**) via an intramolecular cycloaddition reaction of the hypothetical diene intermediate **3c** proposed for the biosynthesis of **1a**.[1] The



	R^1	R^2
3a	H	H
3b	COCH=CHPh	H
3c	H	COCH=CHPh
3d	COCH=CHPh	COCH=CHPh
3e	Ac	H
3f	Ac	COCH=CHPh

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(3) Ganem, B.; Holbert, G. W. *Bioorg. Chem.* **1977**, *6*, 393–396.
(4) Ogawa, S.; Takagaki, T. *J. Org. Chem.* **1985**, *50*, 2356–2359.

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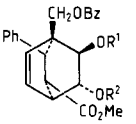
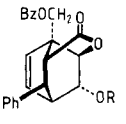
present synthesis also verifies the absolute configuration formerly deduced for **1a**.[1]

Selective esterification of **3a** with 1.7 molar equiv of (*E*)-cinnamoyl chloride afforded three components, which were separated by a silica gel column to give two monoesters **3b** and **3c**, and one diester (**3d**) in 16%, 34%, and 24% yields, respectively. The structures of **3b** and **3c** were established by the ^{1}H NMR spectra, in which the signals due to the protons attached to the carbon atoms bearing the (*E*)-cinnamoyloxy groups appeared as a doublet (J = 7.2 Hz, δ 5.85) and a doublet of doublets (J = 3 and 7 Hz, δ 5.67), respectively. On the other hand, the 2-*O*-acetyl derivative[4] (**3e**) of **3a** was converted into the 3-*O*-(*E*)-cinnamate (**3f**) in 96% yield. The ^{1}H NMR spectrum revealed the signal of the C-3 proton as a doublet of doublets (J = 3.3 and 6.2 Hz) at δ 5.63, in line with that of **3c**.

Intramolecular Diels–Alder reaction of **3c** was carried out in toluene at 70 °C for 4 days to afford a 95% yield of a single adduct. Crystallization from dichloromethane and methanol gave **1a** as needles [mp 203–204 °C; $[\alpha]^{20}_D$ −150° (chloroform)] whose physical properties and ^{1}H NMR spectrum were in good accord with those reported for a natural sample.[1,5] The reaction of **3f** also proceeded smoothly under the similar conditions to afford the acetyl derivative (**1b**) of **1a** in 96% yield. The structure was confirmed by comparison of the ^{1}H NMR spectral data.[1] The acetate **1b** was readily O-deacetylated with *p*-toluenesulfonic acid in dichloromethane and methanol to afford mainly **1a** (54%), together with the methyl esters **4a** (8%) and **4b** (9%). Acetylation of **4a** and **4b** in the usual way afforded the same diacetate (**4c**), the structure of which was assigned by the ^{1}H NMR spectrum. Compound **4a** was convertible into **1a** quantitatively by treatment under more acidic conditions.





	R^1	R^2
4a	Ac	H
4b	H	H
4c	Ac	Ac

5a R = H
5b R = Ac

In order to establish the difference of the reactivity of (*E*)-cinnamoyloxyl functions at C-2 and C-3 in the intramolecular cycloaddition reaction, the diester **3d** was heated in toluene at 70 °C. The reaction gave a sole cycloadduct (**1c**) in 80% yield, the stereochemistry of which was shown to be related to that of **1a** by the ^{1}H NMR spectrum. The stereoelectronic effect seems to control the ease of the cycloaddition reaction of the diene part with the (*E*)-cinnamoyloxyl group. In fact, the intramolecular cycloaddition reaction of **3b** needed a higher temperature (100 °C, 3 days) to afford the adduct **5a** in 65% yield. The structure of **5a** was fully confirmed by the ^{1}H NMR spectra of **5a** and its diacetate (**5b**).

Experimental Section

Melting points were determined in an open capillary tube in a Mel-temp melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded in chloroform-*d* solution with tetramethylsilane as an internal standard. The peak positions are given in δ values. TLC was performed on precoated silica gel 60 F-254 (E. Merck, Darmstadt; 0.2-mm thickness). The silica gel used for column chromatography was Wakogel C-300 (Wako Co., Osaka; 300 mesh). Organic solutions were concentrated below 30 °C under reduced pressure.

Selective Esterification of (2*R*)-*trans*-2,3-Dihydroxy-1-[(benzyloxy)methyl]cyclohexa-4,6-diene (3a). To a solution of **3a**[1] (173 mg, 0.70 mmol) in a mixture of dichloromethane (6 mL) and pyridine (2 mL) was added a solution of (*E*)-cinnamoyl chloride (0.20 g, 1.2 mmol) in dichloromethane (1.2 mL) dropwise at −60 °C for 5 min, and then the reaction mixture was stirred at 0 °C for 1 h, followed by at ambient temperature for 2 h. TLC showed the formation of three components (R_f 0.53, 0.34, and 0.26 in 1:2 ethyl acetate–hexane), together with a trace of **1a**. The mixture was diluted with ethanol and concentrated. The residue was taken up in ethyl acetate and the solution was washed with 1 M hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and water, dried, and then concentrated. The residue was chromatographed on a silica gel column (15 g) with 1:3 ethyl acetate–hexane as eluant.

The first fraction gave 86 mg (24%) of **(2*R*)-*trans*-2,3-bis-[(*E*)-cinnamoyloxy]-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (3d)** as a syrup: $[\alpha]^{19}_D$ −536° (*c* 0.94, $CHCl_3$); ^{1}H NMR (90 MHz, $CDCl_3$) δ 8.10–7.99 (m, 2, phenyl), 7.53–7.30 (m, 13, phenyl), 7.68 (d, 1, J = 15.5 Hz, COCH=C*H*Ph), 7.66 (d, 1, J = 15.5 Hz, COCH=C*H*Ph), 6.38 (d, 2, COC*H*=CHPh), 6.37–5.93 (m, 4, C_2 H, C_4 H, C_5 H, C_6 H), 5.70 (dd, 1, $J_{2,3}$ = 6, $J_{3,4}$ = 3.8 Hz, C_3 H), 4.97 (s, 2 CH_2OBz); mass spectrum, m/z (relative intensity) 506 (M^+, 19), 356 (5.8), 325 (8.8), 131 (100), 105 (14).

The second fraction gave **(2*R*)-*trans*-3-[(*E*)-cinnamoyloxy]-2-hydroxy-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (3c)** (90 mg, 34%) as prisms (ethyl ether): mp 81–83 °C; $[\alpha]^{20}_D$ −331° (*c* 0.63, $CHCl_3$); ^{1}H NMR (90 MHz, $CDCl_3$) δ 8.12–8.01 and 7.54–7.31 (m, 10, phenyl), 7.70 (d, 1, J = 15.5 Hz, COCH=C*H*Ph), 6.41 (d, 1, COC*H*=CHPh), 6.14–5.82 (m, 3, C_4 H, C_5 H, C_6 H), 5.67 (dd, 1, $J_{2,3}$ = 7 and $J_{3,4}$ = 3 Hz, C_3 H), 5.04 (narrow m, 2, CH_2OBz), 4.45 (d, 1, C_2 H), 3.09 (br s, 1, O*H*); mass spectrum, m/z (relative intensity) 376 (M^+, 1.7), 228 (14), 148 (37), 131 (47), 105 (100).

The third fraction gave 43 mg (16%) of **(2*R*)-*trans*-2-[(*E*)-cinnamoyloxy]-3-hydroxy-1-[(benzoyloxy)methyl]-cyclohexa-4,6-diene (3b)** as a syrup: $[\alpha]^{19}_D$ −113° (*c* = 0.91, $CHCl_3$); ^{1}H NMR (90 MHz, $CDCl_3$) δ 8.09–7.97 and 7.51–7.40 (m, 10, phenyl), 7.66 (d, 1, J = 15.5 Hz, COCH=C*H*Ph), 6.67 (d, 1 COC*H*=CHPh), 6.28–6.01 (m, 3, C_4 H, C_5 H, C_6 H), 5.85 (d, 1, $J_{2,3}$ = 7.2 Hz, C_2 H), 4.97 (s, 2, CH_2OBz), 4.55 (dd, 1, $J_{3,4}$ = 1.8 H, C_3 H), 2.78 (br s, 1, O*H*); mass spectrum, m/z (relative intensity) 376 (M^+, 3.7), 358 (6.2), 228 (17), 148 (13), 131 (86), 105 (100).

Intramolecular Diels–Alder Reaction of 3c. Synthesis of Zeylena (1a). A solution of **3c** (40 mg, 0.11 mmol) in toluene (1.5 mL) was heated in a sealed tube at 70 °C for 4 days. TLC (1:1 ethyl acetate–hexane) showed the disappearance of **3c** (R_f 0.59) and the formation of a single component (R_f 0.34), together with a trace of byproduct (R_f 0.62). The mixture was concentrated, and the residue was chromatographed on a silica gel column (3 g) with 2:3 ethyl acetate–hexane as eluant. The main fraction gave 38 mg (95%) of zeylena (**1a**) as crystals. Recrystalization from dichloromethane and methanol gave colorless needles: mp 203–204 °C; $[\alpha]^{20}_D$ −150° (*c* 0.50, $CHCl_3$) [lit.[1] mp 204–205 °C; $[\alpha]^{25}_D$ −136.3°]. The ^{1}H NMR spectrum (270 MHz, $CDCl_3$) was superimposable on that of an authentic sample.[2] Anal. Calcd for $C_{23}H_{20}O_5$: C, 73.40; H, 5.32. Found: C, 73.01; H, 5.40.

(2*R*)-*trans*-2-Acetoxy-3-[(*E*)-cinnamoyloxy]-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (3f). To a solution of **(2*R*)-*trans*-2-acetoxy-3-hydroxyl-1-[(benzoyloxy)methyl]-cyclohexa-4,6-diene[4] (3e)** (235 mg, 0.82 mmol) in dichloromethane (6 mL) was added pyridine (2 mL) followed by a solution of (*E*)-cinnamoyl chloride (0.26 g, 1.6 mmol) in dichloromethane (1.5 mL) at −50 °C. The mixture was stirred at 0 °C for 1 h and then processed as described in the preparations of **3b** and **3c**. The product was purified by chromatography on silica gel (25 g) with 1:5 ethyl acetate–hexane to give 327 mg (96%) of **3f** as a syrup: $[\alpha]^{20}_D$ −436° (*c* 1.4, $CHCl_3$); ^{1}H NMR (90 MHz, $CDCl_3$) δ 8.03–7.80 (m, 2, phenyl), 7.57–7.33 (m, 8, phenyl), 7.68 (d, 1, J = 15.5 Hz, COCH=C*H*Ph), 6.37 (d, 1, COC*H*=CHPh), 6.33–6.00 (m, 3, C_4 H, C_5 H, C_6 H), 5.93 (d, 1, $J_{2,3}$ = 6.2 Hz, C_2 H), 5.63 (dd, 1, $J_{3,4}$ = 3.3 Hz, C_3 H), 4.93 (s, 2, CH_2OBz), 2.02 (s, 3, OAc); mass

(5) Identification with an authentic sample was kindly carried out by Professor Robert B. Bates (University of Arizona), to whom our thanks are due.

spectrum, m/z (relative intensity) 418 (M^+, 4.1), 376 (2), 228 (17), 131 (100), 105 (49).

Intramolecular Diels–Alder Reaction of 3f. Synthesis of Zeylena Acetate (1b). A solution of **3f** (120 mg, 0.29 mmol) in toluene (2.5 mL) was heated in a sealed tube at 70 °C for 4 days. The mixture was concentrated, and the residue was chromatographed on a silica gel column (6 g) with 2:5 ethyl acetate–hexane to give 113 mg (94%) of zeylena acetate (**1b**) as an amorphous solid: $[\alpha]^{21}_D$ −71° (*c* 1.30, $CHCl_3$). The ^1H NMR spectral data were in good accord with those described for an authentic sample.[1] Anal. Calcd for $C_{25}H_{22}O_6$: C, 71.77; H, 5.26. Found: C, 71.83; H, 5.41.

O-Deacetylation of 1b. A mixture of **1b** (110 mg, 0.26 mmol), *p*-toluenesulfonic acid (80 mg, 0.42 mmol), dichloromethane (2 mL), and methanol (12 mL) was stirred at ambient temperature for 3 days. TLC showed the disappearance of **1b** (R_f 0.54) and the formation of one major (R_f 0.34) and two minor components (R_f 0.42 and 0.07) in 1:1 ethyl acetate–hexane. The mixture was neutralized with an excess of sodium hydrogen carbonate and filtered. The filtrate was concentrated, and the residue was fractionated on a silica gel column (5 g) with 1:2 ethyl acetate–hexane as eluant to give first 10 mg (8%) of **methyl (1*S*)-*exo*-5-acetoxy-4-[(benzoyloxy)methyl]-*endo*-6-hydroxy-*exo*-3-phenylbicyclo[2.2.2]oct-8-ene-*endo*-2-carboxyalte (4a)** as a syrup, $[\alpha]^{20}_D$ −68° (*c* 2.0, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.10–7.98 (m, 2, benzoyloxy phenyl) 7.60–7.46 (m, 3, benzoyloxy phenyl), 7.19 (br s, 5, C-phenyl), 6.61 (dd, 1, $J_{1,7}$ = 6.8, $J_{7,8}$ = 8.3 Hz, C_7 H), 5.95 (d, 1, C_8 H), 4.63 (s, 1, C_5 H), 4.50 (d, 1, CH_2OBz), 3.76 (d, 1, J_{gem} = 11.3 Hz, CH_2OBz), 3.88 (d, 1, $J_{2,3}$ = 6.8 Hz, C_3 H), 3.67 (s, 3, ester methyl), 3.60–3.38 (m, 2, C_1 H, C_6 H), 3.10 (br s, 1, OH), 2.67 (dd, 1, $J_{1,2}$ = 2.6 Hz, C_2H), 1.98 (s, 3, OAc); mass spectrum, m/z (relative intensity) 418 (M^+ − 32) (8.0), 376 (4.2), 228 (20), 167 (19), 131 (100), 105 (90). The fraction eluted third was 10 mg (9%) of the dihydroxy ester (**4b**) as a syrup; mass spectrum, m/z (relative intensity) 376 (M^+ − 32) (4.2), 209 (31), 167 (70), 131 (48), 105 (100). The fraction eluted second was 54 mg (54%) of **1a** as a white solid, which was identified with the compound obtained before.

Both compounds **4a** and **4b** were convertible by treatment with acetic anhydride in pyridine into the diacetate (**4c**) quantitatively: syrup, $[\alpha]^{20}_D$ −82° (*c* 1.01, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.11–8.01 (2, m, benzoyloxy phenyl), 7.57–7.48 (m, 3, benzoyloxy phenyl), 7.22 (br s, 5, C-phenyl), 6.67 (dd, 1, $J_{1,7}$ = 7.5 $J_{7,8}$ = 7.8 Hz, C_7 H), 6.05 (d, 1, C_8 H), 5.16 (s, 1, C_5 H), 4.71 (d, 1, $J_{1,6}$ = 3.2 Hz, C_6, H), 4.41 (d, 1, CH_2OBz), 3.75 (d, 1, J_{gem} = 11.5 Hz, CH_2OBz), 3.77 (d, 1, $J_{2,3}$ = 7.5 Hz, C_3, H), 3.67 (s, 3, ester methyl), 3.60 (br m, 1, C_1 H), 2.69 (d, 1, C_2 H), 2.04 (s, 3, OAc), 1.95 (s, 3, 2 OAc); mass spectrum m/z (relative intensity) 492 (M^+, 1.2), 461 (4.5), 419 (10), 330 (12), 270 (9), 228 (75), 105 (100).

(1*R*)-6-[(Benzoyloxy)methyl]-*exo*-10-[(*E*)-cinnamoyloxy]-*exo*-5-phenyl-2-oxatricyclo[4.3.1.0^{4,9}]dec-7-en-3-one [Zeylena (*E*)-Cinnamate] (1c). A solution of **3d** (159 mg, 0.31 mmol) in toluene (4 mL) was heated in a sealed tube at 70 °C for 4 days. The mixture was concentrated, and the residue was purified on a silica gel column (7 g) with 2:3 ethyl acetate–hexane to give 127 mg (80%) of **1c** as an amorphous solid: $[\alpha]^{17}_D$ +26.8° (*c* 1.36, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.10–8.00 (m, 2, phenyl), 7.61–6.97 (m, 13, phenyl), 7.63 (d, 1, *J* = 15.5 Hz, COCH=C*H*Ph), 6.56 (dd, 1, $J_{7,8}$ = 8, $J_{8,9}$ = 6.5 Hz, C_8 H), 6.31 (d, 1, COC*H*=CHPh), 6.04 (d, 1, C_7 H), 5.36 (s, 1, C_{10} H), 4.47 (d, 1, CH_2OBz), 4.01 (d, 1, (J_{gem} = 11.5 Hz, CH_2OBz), 4.42 (dd, 1, $J_{1,4}$ = 1, $J_{1,9}$ = 5 Hz, C_1, H), 3.73 (br q, 1, C_9 H), 3.45 (d, 1, $J_{4,5}$ = 2 Hz, C_5 H), 2.83 (ddd, 1, $J_{4,9}$ = 4.5 Hz, C_4 H); mass spectrum, m/z (relative intensity) 506 (M^+, 15), 356 (6.3), 325 (7.8), 131 (100), 105 (34).

(1*R*)-9-[(Benzoyloxy)methyl]-*exo*-10-hydroxy-*exo*-5-phenyl-2-oxatricyclo[4.3.1.0^{4,9}]dec-7-en-3-one (5a). A solution of **3b** (43 mg, 0.11 mmol) in toluene (2 mL) was heated in a sealed tube at 100 °C for 3 days. The mixture was concentrated, and the product was purified on a silica gel column (2 g) with 1:3 ethyl acetate–hexane to give 28 mg (65%) of **5a** as a colorless syrup: $[\alpha]^{21}_D$ +134° (*c* 0.41, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.12–8.02 (m, 2, 7.67–7.00 (m, 8, phenyl), 6.33–6.27 (m, 2, C_7 H, C_8 H), 4.70 (s, 2, CH_2OBz), 4.23 (s, 1, C_1 H), 4.13 (d, 1, $J_{6,10}$ = 3 Hz, C_{10} H), 3.37–3.23 (m, 2, C_5H, C_6 H), 2.73 (s, 1, C_4 H), 2.15 (br s, 1, OH); mass spectrum, m/z (relative intensity) 376 (M^+, 1.6), 167 (50), 131 (30), 105 (100).

Compound **5a** was converted in the usual way into the acetate (**5b**) in quantitative yield: syrup; $[\alpha]^{24}_D$ +57° (*c* 1.25, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.12–8.02 (m, 2, phenyl, 7.67–7.00 (m, 8, phenyl), 6.25–6.18 (m, 2, C_7 H, C_8 H), 5.08 (d, 1, $J_{6,10}$ = 3 Hz, C_{10} H), 4.70 (s, 2, CH_2OBz), 4.28 (s, 1, C_1 H), 347–3.33 (m, 2, C_5 H, C_6 H), 2.77 (s, 1, C_4 H), 2.00 (s, 3, OAc); mass spectrum, m/z (relative intensity) 418 (M^+, 1.6), 358 (3.1), 328 (5.1), 236 (24), 223 (30), 167 (24), 131 (58), 105 (100).

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Total Synthesis of (±)-Perezone

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A total synthesis of (±)-perezone (1) proceeding in 18% overall yield is described. The sequence starts from 5-bromopiperonal (2) and proceeds by way of 7, making use of an AgO-assisted oxidative dealkylation step to unmask the hydroxy-*p*-quinone-type system characteristic of 1.

Perezone (1), a well-known sesquiterpene quinone, was the first isolated from *Pereziae* sp. in 1852.[1] This rather simple molecule has been the subject of many scientific endeavors,[2] culminating in 1965 in its only reported[3] synthesis which, starting from 3,5-dimethoxytoluene, resulted in a very low overall yield.

In continuation of our research program dealing with the chemistry of sesquiterpene quinones[4–7] we now report

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