The singlet at δ 4.09 characteristic of $BFLH_2$ cannot be detected.

In a similar experiment, BDAF was irradiated in a 1:1 (V:V) mixture of C_6H_{12} and C_6D_{12}. The reaction mixture was analyzed by FI mass spectroscopy for incorporation of deuterium. The 2,3-benzofluorene was 9% monodeuterated, the CYBF derived from C_6H_{12} showed no significant deuterium incorporation and the dimer BBF was 26% monodeuterated.

Irradiation of BDAF in Benzene Containing Methanol. A solution of BDAF (1.3 mg, 5.3×10^{-3} mmol) in benzene (5 mL) containing methyl alcohol (2.5 M) was purged with N_2 and irradiated at 424 nm through an interference filter. When the reaction was complete (UV), the solvent and unreacted alcohol were removed under vacuum, and the residue was analyzed by mass and ^1H NMR spectroscopy. The NMR spectrum shows MBFE (90% by integration against hexamethylbenzene internal standard): ($CDCl_3$) δ 3.1 (s, 3 H), 5.8 (s, 1 H), 7.3-8.1 (m, 10 H); MS (70 eV), *m/e* (relative abundance) 246 (42), 231 (22), 215 (100); molecular ion calcd for $C_{18}H_{14}O$ *m/e* 246.1045, found 246.1044.

Triplet-Sensitized Reaction of BDAF with Methanol. Three samples of BDAF (all 1.0×10^{-3} M, 5 mL) in benzene were prepared, N_2 purged, and irradiated at 424 nm through an interference filter. Sample A contained only BDAF and methyl alcohol (2.5 M). Sample B contained BDAF, methyl alcohol, and benzil (3.6×10^{-2} M). Sample C contained BDAF, methyl alcohol, benzil, and anthracene (1.7×10^{-2} M). After 5 h of irradiation the solvent and unreacted alcohol were removed from the samples under vacuum and the residues analyzed by ^1H NMR spectroscopy with hexamethylbenzene as a standard for integration. The yield of MBFE in sample A was 80%, in sample B 92%, and in sample C 19%. Control experiments showed that there is no ether formation in the absence of light.

Direct Irradiation of BDAF in CH_3CN Containing α-Methylstyrene. An acetonitrile solution (5 mL) of α-methylstyrene (0.81 M) and BDAF (1.9×10^{-3} M) was purged with N_2 and irradiated in a Rayonet photoreactor with 350 nm lamps until the diazo compound was consumed (UV). The solvent and excess α-methylstyrene were removed under vacuum. The ^1H NMR spectrum of the residue showed it to be a mixture of isomeric cyclopropanes formed in essentially quantitative yield as indicated by integration against *p*-dioxane as a standard; ^1H NMR (C_5D_5N) δ 2.45 (t, 1 H), 2.1 (q, 1 H), 1.75 (d, 3 H), 7.2-8.6 (m, 15 H);[27] MS (70 eV), *m/e* (relative abundance) 332 (83), 255 (6), 215 (51); molecular ion calcd for $C_{26}H_{20}$ *m/e* 332.1565, found 332.1570.

In an analogous experiment, (*E*)-β-deuterio-α-methylstyrene (1.76 M) was used and the stereochemistry of the cyclopropanation reaction was determined by ^1H NMR spectroscopy to be 77 ± 13% retention.

Triplet-Sensitized Photolysis of BDAF in CH_3CN Containing α-Methylstyrene. An acetonitrile solution (10 mL) of BDAF (2.0×10^{-3} M), α-methylstyrene (0.73 M) and benzil (6.6×10^{-2} Me was purged with N_2 and irradiated through a 424-nm interference filter. The solvent and unreacted styrene were removed under vacuum. The ^1H NMR spectrum of the residue revealed formation of the expected cyclopropane in greater than 80% yield.

In an analogous experiment, (*E*)-β-deuterio-α-methylstyrene (0.70 Me was used. The stereochemistry of the cyclopropanation reaction was found to be the same as in the direct irradiation.

Control experiments showed that benzil is not quenched significantly by the styrene at the concentrations used and that the styrene is not significantly isomerized under these conditions.

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(27) Residual α-methylstyrene and residual hydrogen in the deuterated solvents complicate integration of the aromatic region for this compound. Subtraction of the solvent contribution gives an aromatic proton count of 13 H.

Total Synthesis of (+)-Pipoxide and (+)-β-Senepoxide and Their Diene Precursors

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(2*R*)-*trans*-2,3-Diacetoxy-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (**6**), a diene precursor in the biosynthesis of highly oxygenated cyclohexane epoxides, has first been totally synthesized from the bromo lactone **16** derived from (1*S*)-*endo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid (**15**), adapting the procedure formerly used for the preparation of racemic **6**. Chemical conversions of **6** into the other dienes (**10** and **13**) and epoxides, (+)-pipoxide (**4**) and (+)-β-senepoxide (**5**), have also been achieved. The present syntheses constitute formal total synthesis of (−)-senepoxide (**2**), (−)-tingtanoxide (**3**), and (−)-zeylenol (**14**).

The plant metabolites (+)-crotepoxide (**1**),[1] (−)-senepoxide (**2**),[2] and (+)-pipoxide (**4**)[3] belong to a family of highly oxygenated cyclohexane epoxides exhibiting interesting biological activity. Recent extensive work on plants in the *Uvaria* genus[4,5] has led to the discovery of intermediate, the "missing link", dienes **6**, **10**, and **13**, which are key substances for elucidation of the biogenesis of the compounds of this class, and further added two new epoxides, (−)-tingtanoxide (**3**) and (+)-β-senepoxide (**5**), to

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(3) Singh, J.; Dhar, K. J.; Atal, C. K. *Tetrahedron* **1970**, *26*, 4403.

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(5) Kodopinid, M.; Sadavongvivad, C.; Thebtaranonth, C.; Thebtaranonth, Y. *Tetrahedron Lett.* **1983**, *24*, 2019. (−)-Senepoxide (**2**) was obtained, although in a small yield, by epoxidation of the diene **6**. (−)-Tingtanoxide (**3**) was obtained by epoxidation of the diene **10**.

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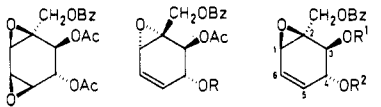
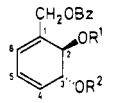
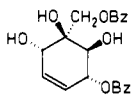
Chart I



1 2 R = Ac 3 R = Bz

	R^1	R^2
4	H	Bz
5	Ac	Ac





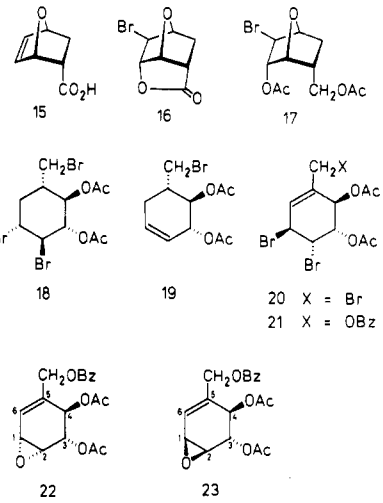
14

	R^1	R^2
6	Ac	Ac
7	Ac	H
8	H	Ac
9	H	H
10	Ac	Bz
11	Bz	Bz
12	Bz	H
13	H	Bz

this family. In this paper, we describe the first total synthesis of optically active **6**, important also as a useful synthetic intermediate, from the bromo lactone **16** derived from (1*S*)-*endo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid (**15**)[6,7] and successful chemical conversions of **6** into **5**, **10**, and **13**. Compound **4** was prepared in good yield by direct epoxidation of **13**. Present syntheses of **4**, **6**, and **10** constitute a formal total synthesis of (−)-zeylenol (**14**),[8,9] **2**,[5] and **3**,[4,5] respectively, and correlation of the absolute configurations of all the dienes and epoxides have been established.

Compound **6** was synthesized from **16**, whose absolute configuration was determined by X-ray analysis,[7] according to the procedure formerly used for the preparation of racemic **6**.[10] Thus, **16**, reduced with lithium aluminum hydride followed by acetylation, gave the diacetate **17**[11] in 84% yield. Cleavage of the anhydro ring of **17** with hydrogen bromide in acetic acid at 90 °C gave crystalline tribromide **18** (71% yield),[11] which was treated with zinc dust in acetic acid at 70 °C to give the bromide **19**[11] in 80% yield. Compound **19** was then treated with *N*-bromosuccinimide in carbon tetrachloride in the presence of α,α-azobis(isobutyronitrile) at 80 °C to give the tribromide **20**,[10,12] which was, without purification, treated with sodium benzoate in *N*,*N*-dimethylformamide to give crystalline dibromide **21** (44% yield).[10] Dehalogenation of **21** with zinc dust in ethanol at 70 °C gave, after chromatography on silica gel, a syrupy diene **6** in 91% yield. The structure of **6** was confirmed by ^{1}H NMR and mass spectrometry,[6] and its specific rotation was in accord with that reported for the natural product.[5]

Chart II



15 16 17

18 19 20 X = Br 21 X = OBz

22 23

Epoxidation of **6** with a slight excess of *m*-chloroperoxybenzoic acid in 1,2-dichloroethane in the presence of phosphate buffer solution (pH 8) was carried out at room temperature for 15 h. The formation of three compounds was detected by TLC. Fractionation of the mixture with a silica gel column gave the monoepoxides **5**, **22**, and **23** in 19%, 24%, and 14% isolated yields, respectively. Their structures were assigned by comparing the ^{1}H NMR spectra with those of known racemic modifications.[10] The optical rotation of **5** was found to agree with the value described for the natural product.[5]

Selective O-deacetylation of **6** was attempted by treatment with *p*-toluenesulfonic acid in methanol at room temperature. After three days, when **6** had been consumed, the reaction was quenched by addition of sodium hydrogen carbonate, and the products were separated by chromatography on silica gel. Two monoacetates (**7**, 19% and **8**, 2%) were obtained, along with the dihydroxy compound (**9**, 47%). Compounds **7** and **8** could readily be differentiated by their ^{1}H NMR spectra, in which the signals due to the protons attached to the carbon atoms carrying the acetoxy groups appeared as a doublet (δ 5.73, J = 7.2 Hz) and a doublet of doublets (δ 5.53, J = 3 and 7.8 Hz). Compound **7** was benzoylated in the usual way to give a dibenzoate (**10**) as a syrup in 95% yield. The physical and spectroscopic properties of **10** were identical with those reported for the natural product.[5]

Selective benzoylation of **9** was carried out to achieve an effective synthesis of **13**. A solution of **9** in dry pyridine was treated with a molar equivalent of benzoyl chloride at −5 °C. When **9** had been consumed, the products were isolated by chromatography on silica gel to give two dibenzoates (**12**, 9% and **13**, 46%), along with a 35% yield of the tribenzoate **11**. The ^{1}H NMR spectrum and optical rotation of **13** were identical with those of an authentic sample.[4] The ^{1}H NMR spectra of **12** and **13** revealed signals of the protons attached to the ring carbon atoms bonded to the benzoyloxy groups as a doublet (δ 5.97, J = 7.1 Hz) and a doublet of doublets (δ 5.77, J = 3.3 and 7.4 Hz) and are consistent with the assigned structures.

Direct epoxidation of **13** under the conditions used for the preparation of **5** gave crystalline **4** in 87% yield. The ^{1}H NMR spectrum and optical rotation of **4** were identical with those of the natural product.[4,13]

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(9) Schulte, G. R.; Ganem, B. *Tetrahedron Lett.* **1982**, *23*, 4299. (−)-Zeylenol (**14**) could be obtained by hydrolysis of (+)-pipoxide (**4**).
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(11) Ogawa, S.; Kasahara, I.; Suami, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 118.
(12) The conversion of **19** to **20** would be rationalized as follows: The intermediate allyl bromide initially formed undergoes dehydrobromination followed by addition of bromine generated in situ, or vice versa.
(13) Holbert, G. W.; Ganem, B.; Van Engen, D.; Clardy, J.; Borsub, L.; Chantrapromma, K.; Sadavongvivad, C.; Thebtaranonth, Y. *Tetrahedron Lett.* **1979**, 715. The revised structure of **4** was described, and **4** was totally synthesized by epoxidation of **9** followed by selective benzoylation. Compound **4** was also obtained by epoxidation of **13**.[4]

Experimental Section[14]

Melting points were determined in an open capillary tube in a MEL-TEMP melting point apparatus and are uncorrected. ^1H NMR spectra were recorded at 90 MHz 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 plates (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 dried over anhydrous sodium sulfate and concentrated below 30 °C under reduced pressure. The structures of new optically active compounds synthesized were assigned on the basis of the ^1H NMR spectra, when their corresponding racemic modifications were known and available.

(1*S*)-*endo*-3-Acetoxy-*endo*-5-(acetoxymethyl)-*exo*-2-bromo-7-oxabicyclo[2.2.1]heptane (17). (1*S*)-*exo*-9-Bromo-2,7-dioxatricyclo[4.2.1.$0^{4,8}$]nonan-3-one (**16**)[7] (5.0 g, 23 mmol) was reduced with lithium aluminum hydride (1.0 g, 26 mmol) in tetrahydrofuran (40 mL) as in the preparation of racemic **17**.[11] The crude product was recrystallized from ethanol to give 5.9 g (84%) of **17** as prisms: mp 76–78 °C; $[\alpha]^{22}_D$ + 54° (*c* 1.19, C_2H_5OH). The ^1H NMR spectrum was identical with that of racemic **17**.

Anal. Calcd for $C_{11}H_{15}BrO_5$: C, 43.02; H, 4.92; Br, 26.02. Found: C, 43.20; H, 4.91; Br, 26.30.

(1*R*)-(1,3,5/2,4)-3,4-Diacetoxy-1,2-dibromo-5-(bromomethyl)cyclohexane (18). Compound **17** (3.0 g, 9.8 mmol) was treated with 20% hydrogen bromide in acetic acid (15 mL) in a sealed tube at 90 °C for 20 h. The reaction mixture was processed as in the preparation of racemic **18**,[11] and the product was recrystallized from ethanol to give 3.2 g (74%) of **18** as prisms: mp 126–128 °C; $[\alpha]^{24}_D$–1.4° (*c* 1.35, $CHCl_3$). The ^1H NMR spectrum was identical with that of racemic **18**.

Anal. Calcd for $C_{11}H_{15}Br_3O_4$: C, 29.30; H, 3.35; Br, 53.16. Found: C, 29.17; H, 3.33; Br, 52.81.

(1*R*)-(1,3/2)-2,3-Diacetoxy-1-(bromomethyl)cyclohex-4-ene (19). Compound **18** (5.0 g, 11 mmol) was treated with zinc dust (2.9 g, 44 m atom) in acetic acid as in the preparation of racemic **19**.[10] The product was purified by a silica gel column (20 g) with chloroform as eluant to give 2.6 g (80%) of **19** as needles (from ethanol): mp 56–58 °C; $[\alpha]^{19}_D$–2.2° (*c* 1.25, $CHCl_3$). The ^1H NMR spectrum was identical with that of racemic **19**.

Anal. Calcd for $C_{11}H_{15}BrO_4$: C, 45.38; H, 5.19; Br, 27.45. Found: C, 45.11; H, 5.12; Br, 27.21.

Reaction of 19 with *N*-Bromosuccinimide in Carbon Tetrachloride. Compound **19** (2.5 g, 8.6 mmol) was treated with *N*-bromosuccinimide (3.1 g, 17 mmol) in carbon tetrachloride in the presence of α,α-azobis(isobutyronitrile) as in the preparation of racemic **(1,4/2,3)-3,4-diacetoxy-1,2-dibromo-5-(bromomethyl)cyclohex-5-ene (20).**[10] Crude **20** was treated with sodium benzoate (1.3 g, 9 mmol) in *N*,*N*-dimethylformamide,[10] and the product was crystallized from ethanol to give 1.86 g (44% based on **19**) of **(1*S*)-(1,4/2,3)-3,4-diacetoxy-5-[(benzoyloxy)methyl]-1,2-dibromocyclohex-5-ene (21)** as needles: mp 129-130 °C; $[\alpha]^{21}_D$ + 29.4° (*c* 0.98, $CHCl_3$). The ^1H NMR spectrum was identical with that of racemic **21**.

Anal. Calcd for $C_{18}H_{18}Br_2O_6$: C, 44.11; H, 3.70; Br, 32.60. Found: C, 43.86; H, 3.66; Br, 32.31.

(2*R*)-*trans*-2,3-Diacetoxy-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (6). To a stirred solution of **21** (0.60 g, 1.22 mmol) in ethanol (20 mL) was added zinc dust (0.36 g, 5.5 m atom) in three portions at 70 °C during 10 min. The reaction mixture was stirred for 30 min at the same temperature. TLC showed the formation of one major component (R_f 0.58) and three minor components (R_f 0.23, 0.17, and 0.05) along with a trace of **21** (R_f 0.65) in 2-butanone–toluene (1:8, v/v). An insoluble matter was filtered off, and the filtrate was concentrated. The residue was treated with acetic anhydride (10 mL) and pyridine (10 mL) at room temperature for 2 h. The mixture was concentrated, and the residue was chromatographed on a silica gel column (20 g) with 2-butanone–toluene (1:10, v/v) as eluant. The main fraction gave 0.37 g (91%) of **6** as a syrup: $[\alpha]^{22}_D$–275° (*c* 1.59, $CHCl_3$) [lit.[5] $[\alpha]^{22}_D$ –233° (*c* 0.38, $CHCl_3$)]; mass spectrum, calcd for $C_{18}H_{18}O_6$, *m/z* 330.1101, found, *m/z* 330.1100. The IR ($CHCl_3$), ^1H NMR ($CDCl_3$), and UV (C_2H_5OH) spectral data were identical with those described for the natural product.[5]

Epoxidation of 6 with *m*-Chloroperoxybenzoic Acid (MCPBA). To a mixture of **6** (283 mg, 0.86 mmol), 1,2-dichloroethane (8 mL), and phosphate buffer solution (pH 8) (10 mL) was added MCPBA (212 mg, 0.86 mmol, purity 70%) in three portions, and the mixture was stirred at room temperature for 15 h. TLC showed the disappearance of **6** and the formation of three components (R_f 0.51, 0.45, and 0.38) in 2-butanone-toluene (1:8, v/v). The mixture was diluted with chloroform (100 mL), and the solution was washed successively with 10% aqueous sodium sulfite, aqueous sodium hydrogen carbonate, and water, and dried. The solvent was removed, and the residue was chromatographed on a silica gel column (20 g) with 2-butanone–toluene (1:25, v/v) as eluant. The first fraction gave 57 mg (19%) of **(1*R*)-3,4-di-*O*-acetyl-1,2-anhydro-(1,2,3/4)-2-*C*-[(benzoyloxy)methyl]-5-cyclohexene-1,2,3,4-tetrol [(+)-β-senepoxide] (5)** as needles (from ethanol): mp 68–69 °C; $[\alpha]^{23}_D$ +94° (*c* 1.11, $CHCl_3$) [lit.[5] mp 72–73 °C; $[\alpha]^{25}_D$ +62° (*c* 0.55, $CHCl_3$)]. The ^1H NMR spectrum was superposable on that of an authentic natural product.[5]

Anal. Calcd for $C_{18}H_{18}O_7$: C, 62.42; H, 5.24. Found: C, 62.19; H, 5.45.

The second fraction gave 71 mg (24%) of **(1*R*)-3,4-di-*O*-acetyl-1,2-anhydro-(1,2,3/4)-5-[(benzoyloxy)methyl]-5-cyclohexene-1,2,3,4-tetrol (22)** as prisms (from ethanol): mp 88–89 °C; $[\alpha]^{24}_D$ +42° (*c* 1.06, $CHCl_3$). The ^1H NMR spectrum was superposable on that of racemic **22**.[10]

Anal. Calcd for $C_{18}H_{18}O_7$: C, 62.42; H, 5.24. Found: C, 62.57; H, 5.34.

The third fraction gave 43 mg (14%) of **(1*S*)-3,4-di-*O*-acetyl-1,2-anhydro-(1,2,4/3)-5-[(benzoyloxy)methyl]-5-cyclohexene-1,2,3,4-tetrol (23)** as prisms (from ethanol): mp 105–106 °C; $[\alpha]^{20}_D$ –146° (*c* 1.14, $CHCl_3$). The ^1H NMR spectrum was superposable on that of racemic **23**.[10]

Anal. Calcd for $C_{18}H_{18}O_7$: C, 62.42; H, 5.24. Found: C, 62.16; H, 5.20.

O-Deacetylation of 6. A mixture of **6** (248 mg, 0.75 mmol) and *p*-toluenesulfonic acid (60 mg, 0.32 mmol) in methanol (20 mL) was stirred at 15–20 °C for 3 days. TLC showed the formation of two major components (R_f 0.24 and 0.10) and one minor component (R_f 0.32) in ethyl acetate–hexane (1:2, v/v). The reaction mixture was treated with excess sodium hydrogen carbonate, filtered, and concentrated. The product was fractionated by a silica gel column (15 g) with ethyl acetate–hexane (1:3, v/v) as eluant. The first fraction gave 5 mg (2%) of **(2*R*)-*trans*-3-acetoxy-2-hydroxy-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (8)** as a syrup: $[\alpha]^{25}_D$ –132° (*c* 0.55, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.12–8.02 (m, 2) and 7.58–7.43 (m, 3) (phenyl), 6.12–5.87 (m, 3, C_4 H, C_5 H, C_6 H), 5.53 (dd, 1, $J_{2,3}$ = 7.8, $J_{3,4}$ = 3 Hz, C_3 H), 5.04 (s, 1) and 4.99 (s, 1) (CH_2OBz), 4.50 (d, 1, C_2 H), 2.77 (br s, 1, OH), 2.07 (s, 3, OAc); mass spectrum, calcd for $C_{16}H_{11}O_5$, *m/z* 288.0997, found, *m/z* 288.0992.

The second fraction gave 42 mg (19%) of **(2*R*)-*trans*-2-acetoxy-3-hydroxy-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (7)** as a syrup: $[\alpha]^{24}_D$ –150° (*c* 1.22, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.12–8.00 (m, 2) and 7.60–7.43 (m, 3) (phenyl), 6.27–5.97 (m, 3, C_4 H, C_5 H, C_6 H), 5.73 (d, 1, $J_{2,3}$ = 7.2 Hz, C_2 H), 4.92 (s, 2, CH_2OBz), 4.47 (dd, 1, $J_{3,4}$ = 2.7 Hz, C_3 H), 2.50 (br s, 1, OH), 2.05 (s, 3, OAc); mass spectrum, calcd for $C_{16}H_{16}O_5$, *m/z* 288.0996, found, *m/z* 288.0992.

The third fraction gave 87 mg (47%) of **(2*R*)-*trans*-2,3-dihydroxy-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (9)** as a syrup: $[\alpha]^{24}_D$ –111° (*c* 1.47, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.12–8.00 (m, 2) and 7.57–7.40 (m, 3) (phenyl), 6.02–5.88 (br m, C_4 H, C_5 H, C_6 H), 5.13 (d, 1) and 4.87 (d, 1) (J_{gem} = 6.8 Hz, CH_2OBz), 4.50 (br s, 2, C_2 H, C_3 H), 3.20 (br s, 2, OH); mass spectrum, calcd for $C_{14}H_{14}O_4$, *m/z* 246.0891, found, *m/z* 246.0878.

(2*R*)-*trans*-2-Acetoxy-3-(benzoyloxy)-1-[(benzoyloxy)methyl]cyclohexa-4,6-diene (10). Compound **7** (24 mg, 0.08 mmol) was treated with benzoyl chloride (20 μL, 0.25 mmol) in pyridine (1 mL) at –5 °C for 10 min. The reaction mixture was diluted with ethyl acetate (10 mL), and the solution was washed

(14) The nomenclature and numbering of cyclitols, **4**, **5**, **22**, and **23**, used in this paper follow the IUPAC-IUB 1973 Recommendations for Cyclitol (*Pure Appl. Chem.* **1974**, *37*, 285).

with 1 M hydrochloric acid, aqueous sodium hydrogen carbonate, and water and dried. The solvent was removed, and the residue was purified by a silica gel column (4 g) with ethyl acetate–hexane (1:15, v/v) to give 31 mg (95%) of **10** as a syrup: $[\alpha]^{27}_D$ −335° (*c* 1.21, $CHCl_3$) [lit.[5] $[\alpha]^{28}_D$ −298° (*c* 0.37, $CHCl_3$)]; mass spectrum, calcd for $C_{23}H_{20}O_6$, *m/z* 392.1258, found, *m/z* 392.1256. The IR ($CHCl_3$), ^1H NMR ($CDCl_3$), and UV (C_2H_5OH) spectral data were identical with those described for the natural product.[5]

Selective Benzoylation of 9. To a stirred solution of **9** (66 mg, 0.27 mmol) in pyridine (3 mL) was added benzoyl chloride (60 μL, 0.51 mmol) in three portions at −5 °C during 30 min. TLC showed the formation of three components (R_f 0.62, 0.43, and 0.33), along with a trace of **9** (R_f 0.10) in ethyl acetate–hexane (1:2, v/v). The reaction mixture was processed in the usual way, and the products were fractionated by a silica gel column (6 g) with ethyl acetate–hexane (1:4, v/v). The first fraction gave 42 mg (35%) of **(2*R*)-*trans*-2,3-bis(benzoyloxy)-1-[(benzoyloxy)methyl]-cyclohexa-4,6-diene (11)** as a syrup: $[\alpha]^{25}_D$ −395° (*c* 0.88, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.07–7.96 (m, 6) and 7.55–7.32 (m, 9) (phenyl), 6.43–6.13 (m, 4, C_2 H, C_4 H, C_5 H, C_6 H), 5.87 (dd, 1, $J_{3,4}$ = 3.5, $J_{2,3}$ = 6.1 Hz, C_3 H), 5.00 (s, 2, CH_2OBz); mass spectrum (relative intensity), 332 (M^+ − $PhCO_2H$, 12), 122 ($PhCO_2H$, 7), 105 (PhCO, 100).

The second fraction gave 43 mg (46%) of **(2*R*)-*trans*-3-(benzoyloxy)-1-[(benzoyloxy)methyl]-2-hydroxycyclohexa-4,6-diene (13)** as needles (from benzene–hexane): mp 79.5–81 °C; $[\alpha]^{25}_D$ −297° (*c* 1.19, $CHCl_3$) [lit.[4] mp 90–91 °C; $[\alpha]^{25}_D$ −276° (*c* 0.145, $CHCl_3$)]. The ^1H NMR spectrum was superposable on that of the natural product.[4]

Anal. Calcd for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 71.70; H, 5.25.

The third fraction gave 8 mg (9%) of **(2*R*)-*trans*-2-(benzoyloxy)-1-[(benzoyloxy)methyl]-3-hydroxycyclohexa-4,6-diene (12)** as a syrup: $[\alpha]^{25}_D$ −119° (*c* 0.33, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 8.08–7.91 (m, 4) and 7.57–7.33 (m, 6) (phenyl), 6.33–6.04 (m, 3, C_4 H, C_5 H, C_6 H), 5.97 (d, 1, $J_{2,3}$ = 7.1 Hz, C_2 H), 4.97 (br s, 2, CH_2OBz), 4.63 (dd, 1, $J_{3,4}$ = 2.7 Hz, C_3 H), 2.37 (br s, 1, OH); mass spectrum (relative intensity), 332.1048 (M^+ − H_2O, 100) (calcd for $C_{21}H_{16}O_4$, 332.1047).

(1*R*)-1,2-Anhydro-4-*O*-benzoyl-(1,2,3/4)-2-*C*-[(benzoyloxy)methyl]-5-cyclohexene-1,2,3,4-tetrol [(+)-Pipoxide] (4). To a stirred mixture of **13** (43 mg, 0.12 mmol) in dichloromethane (1.5 mL) and phosphate buffer solution (pH 8) (2 mL) was added dropwise a solution of MCPBA (30 mg, 0.12 mmol, purity 70%) in dichloromethane (1 mL) at 0 °C, and the mixture was stirred for 1 h at the same temperature. The reaction mixture was processed in the usual way to give 39 mg (87%) of **4** as needles (from benzene–hexane): mp 150–151 °C; $[\alpha]^{20}_D$ +48.6° (*c* 0.76, $CHCl_3$) [lit.[3] mp 152–154 °C; $[\alpha]^{20}_D$ +24.5° (*c* 0.20, $CHCl_3$); lit.[4] $[\alpha]^{20}_D$ +37.9° (*c* 0.16, $CHCl_3$); lit.[12] mp 152 °C, $[\alpha]^{23}_D$ +53° (*c* 0.02, $CHCl_3$)]; UV max (C_2H_5OH) 276 mm (ε 2340); IR (KBr) 3450 (OH), 1710 (ester C=O) cm^{-1}. The ^1H NMR spectrum was superposable on that of the natural product.[4]

Anal. Calcd for $C_{21}H_{18}O_6$: C, 68.57; H, 4.95. Found: C, 68.32; H, 5.04.

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Synthesis of (20*R*,25*R*)-Cholest-5-ene-3β,26-diol and the Occurrence of Base-Catalyzed 1,5-Hydride Shift in a Steroidal 1,5-Ketol[1]

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Details are presented for the preparation of (20*R*,25*R*)-cholest-5-ene-3β,26-diol (**2**, "26-hydroxycholesterol"). Kryptogenin diacetate (**8**) was converted to **2** in 39% yield by successive removal of the C-16 and C-22 carbonyl functions (cycloethylene dithioketal formation followed by Raney nickel desulfurization). 22-Oxocholest-5-ene-3β,26-diol (**17**) was shown to be an intermediate in a previous preparation of **2**, and it was shown to be a source of C-25 epimerization and byproducts in that procedure. The products seen in the Wolff–Kishner reduction of **17** are explained by base-catalyzed equilibration of **17** with 26-oxocholest-5-ene-3β,22-diol (**23**). This equilibration by base-catalyzed 1,5-hydride shift was demonstrated by deuterium labeling. ^{13}C and ^1H NMR correlations were developed for the above compounds.

(20*R*,25*R*)-Cholest-5-ene-3β,26-diol, "26-hydroxycholesterol", an intermediate in bile acid biosynthesis, is a potentially important factor in the study of atherosclerosis. It is a potent inhibitor of cholesterol synthesis in vitro.[2] In human serum it is present in free and esterified form in both the low density (LDL) and high density lipoproteins (HDL). It is a constituent of human atherosclerotic plaque.[3] Because of these facts and because of the proposal that oxygenated sterols in LDL might be involved in the regulation of cholesterol synthesis through mediation of the binding of LDL to a cell surface receptor,[4] we decided to prepare 26-hydroxycholesterol for biological investigation.[5]

Microsomal hydroxylation at C-26 in cholesterol gives the 25*R* diastereoisomer,[6] and material isolated from hu-

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(5) We thank Professor Norman B. Javitt, New York University Medical Center, for bringing this problem to our attention.

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