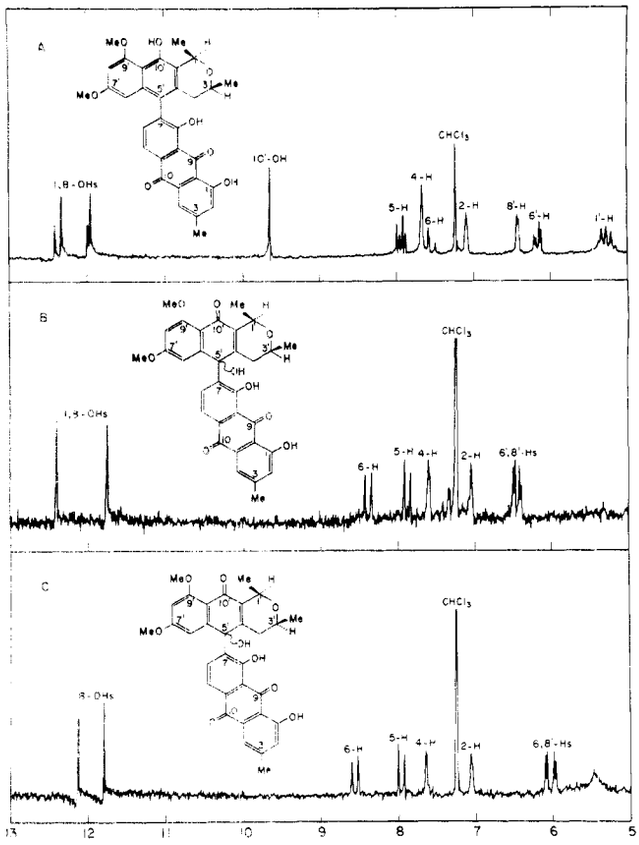

Figure 1. (A) Partial ^1H NMR spectrum of **3** exhibiting resonances of two atropisomers; (B) partial ^1H NMR spectrum of the nonpolar isomer of the diasteriomeric alcohol pair (**4**) obtained by air oxidation of **2**; (C) the partial ^1H NMR of the corresponding polar isomer (**4**).

hydroxy in the starting material[2] (see Figure 1A) was absent. The resonances due to two methoxy groups and the A′-ring aromatic AB system as well as signals due to the corresponding protons in the A′,C′, and C rings of **3** were present in each and could be related to the corresponding signals in **3**.

These results lead us to assign general structure **4** to the new products, designated nonpolar and polar in accord with their relative chromatographic mobilities (see Experimental Section). The existence of two very similar isomers is then due to (a) air oxidation of the ABC system with creation of an anthraquinone moiety and (b) the creation of a new chiral center with hydroxylation at the 5′ position. Since it has been established[2] that the two C-methyl substituents of ring A′ are cis diequatorially related to one another, a chiral center at the 5′ position would place the 5′-hydroxy either cis or trans to the C-methyls (**4a** and **4b**, respectively).

The differences in the ^1H NMR spectra of the nonpolar and polar 5′-hydroxy isomers (**4**) are appreciable (compare Figures 1B and 1C) and must result from differences in hydrogen bonding (5′-OH to O-8)[7] and/or conformational differences. We have been unable to account for the observed differences by inspection of molecular models and, therefore, have not assigned stereochemistries at C-5′ to the isolated isomer pair.

Experimental Section

Isolation of Isomeric 7-[3′,4′-Dihydro-7′,9′-dimethoxy-1′,3′-dimethyl-5′-hydroxy-10′-oxo-1′*H*-naphtho[2′,3′-*c*′]pyran-5′-yl]-1,8-dihydroxy-3-methylanthracene-4,10-diones (4). A methanol filtrate retained following recrystallization of **2**[2] was allowed to stand at room temperature in contact with air for ~4 months. At the end of this time thin layer chromatography showed the presence of several new products. By chromatography on silica gel using chloroform for elution, two components, assigned general structure **4**, were isolated in approximately equal amounts (~5 mg).

The first compound to elute, designated the nonpolar isomer, exhibited spectral data: MS *m/e* 556.1719 ($C_{32}H_{28}O_9$, M^+ ·), *m/e* 541, 526, 511, 496, 482; UV λ_{max} (MeOH) 228, 258, 290, 330, 435 nm; IR ν_{max} (KBr) 3440, 1630, 1603 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.44, 11.79 (1, 8-OH's), 8.38 (d, J = 8 Hz, 6-H), 7.87 (d, J = 8 Hz, 5-H), 7.59 (d, J = 1 Hz, 4-H), 7.05 (d, J = 1 Hz, 2-H), 6.49, 6.40 (both d, J = 2 Hz, 6′, 8′-H's), 4.90 (m, 1′-H), 3.90, 3.71 (OMes), 2.42 (3-Me), 1.47 (d, J = 6 Hz, 1′-Me), 1.17 (d, J = 6 Hz, 3′-Me).

The polar isomer exhibited: MS *m/e* 556.1711 ($C_{32}H_{28}O_9$, M^+ ·), 541, 526, 511, 496, 482; UV λ_{max} (MeOH) 228, 258, 290, 330, 435 nm; IR ν_{max} (KBr) 3390, 1625, 1603 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.18, 11.84 (1,8-OHs), 8.57 (d, J = 8 Hz, 6-H), 7.96 (d, J = 8 Hz, 5-H), 7.64 (d, J = 1 Hz, H-4), 7.07 (d, J = 1 Hz, H-2), 6.09, 5.98 (both d, J = 2 Hz, 6′-,8′-H's), 5.48 (m, 1′-H), 3.69, 3.65 (OMes), 2.45 (3-Me), 1.43 (d, J = 6 Hz, 1′-Me), 1.21 (d, J = 6 Hz, 3′-Me).

Acknowledgment. We thank the National Institute for Neurological Disease and Stroke (NS 10484) for financial support.

Registry No.—**2**, 56709-27-4; **3**, 56678-20-7; 4 isomer 1, 64957-52-4; 4 isomer 2, 65024-71-7.

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Voleneol Diacetate: a New Sesquiterpenoid from *Lepidotrichilia volensii* Leroy (Meliaceae)

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As the result of a phytochemical investigation of the chloroform extract of the stem bark of *Lepidotrichilia volensii* Leroy (Meliaceae),[1] the diacetate of a new sesquiterpenediol was obtained and characterized as I.

Discussion

One of the constituents of the chloroform extract of *Lepidotrichilia volensii* Leroy was an oil which on acetylation yielded a beautifully crystalline new substance with the molecular formula $C_{19}H_{30}O_4$. The mass spectrum of this diacetate indicated a parent peak at *m/e* 322. The fragmentation pattern was consistent wih successive losses of acetic acid [*m/e* 262 and 202 (base)] and the loss of a methyl (187) and isopropyl radical (159) from the base fragment.

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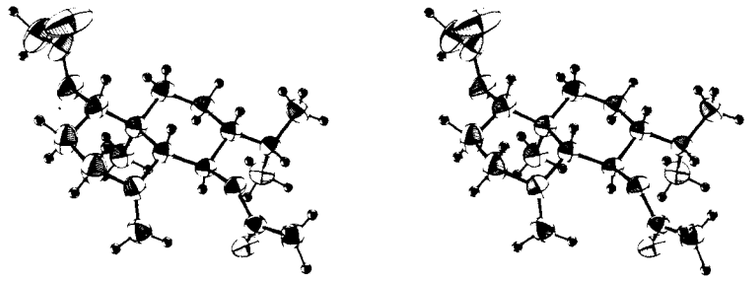
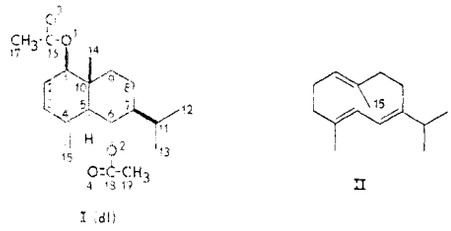


Figure 1. Stereoscopic view of a voleneol diacetate (I) molecule. Hydrogen atoms are shown as spheres and other atoms as 50% probability ellipsoids.



I (dl)

II

The ^{1}H NMR spectrum indicated the presence of a terminal methylene group (δ 4.6 and 4.8), a quaternary methyl group (δ 0.73), two isopropyl methyls (d, δ 0.86 and 0.91, J = 6 Hz), and two acetyl methyls (δ 2.0 and 2.1). The methinyl protons on C-6 and C-1 appeared as a triplet broadened by virtual coupling (δ 5.1, J = 10 Hz) and a doublet of doublets (δ 4.7, J = 5, 10 Hz), respectively. Due to the large coupling constants, the C-6 proton must be axial and split by two adjacent axial protons at C-5 and C-7. After deacetylation with potassium bicarbonate in methanol, a monoacetate was formed in which the doublet of doublets absorbed upfield at δ 3.43 and is thus the C-6 monoacetate. Since the observed rotation of voleneol diacetate was 0°, the compound appeared to be a racemic mixture.

The structure of voleneol diacetate was conclusively determined to be I (*dl*) by x-ray crystallography. Table I lists fractional coordinates, and Figure 1 depicts the molecule. The compound is a *trans*-decalin with both rings in the chair conformation and the acetoxyl and isopropyl substituents equatorial. The isopropyl group adopts the staggered conformation about the C(7)–C(11) bond which puts the hydrogen on C-11 near the bulky acetoxyl group on C-6.

The most surprising feature is that this natural product derivative, with five asymmetric centers, occurs in racemic form, suggesting that it comes from an achiral or easily racemized precursor by nonenzymatic reactions which could occur in the plant, during silica gel chromatography or on acetylation. A reasonable achiral precursor is germacrene C(II), an optically inactive sesquiterpene found as the main constituent of the seeds of *Kadsura japonica* and a key intermediate in the biosynthesis of germacrene D and thus the cadinane family of sesquiterpenoids.[2] Between II and voleneol diacetate (I) an oxidation step is required and probably occurs as a last enzyme-catalyzed step; this could involve allylic oxidation to an optically inactive alcohol such as 15-hydroxygermacrene C or to something optically active with could later easily racemize, such as the allylic rearrangement product of 15-hydroxygermacrene C. Hydrations and cyclizations catalyzed by weak acid could convert this oxidized germacrene derivative to the eudesmoid structure observed.

Experimental Section[3]

Extraction Procedure. The dried and ground stem bark (8 kg) of *Lepidotrichilia volensii* was defatted with petroleum ether and then extracted exhaustively in a Lloyd-type extractor with ethanol. The air-dried ethanol extract was partitioned between chloroform and water (1:1) to yield 460 g of air-dried chloroform extract. The chloroform extract was triturated in ether and the ether-soluble fraction was subjected to a series of silica gel column chromatographies and preparative thick-layer chromatographies to yield 60 mg of an oil.

Table I. Fractional Coordinates of Nonhydrogen Atoms, with Standard Deviations in Parentheses

Atom	x/a	y/b	z/c
O-1	0.0624 (1)	1.2660 (2)	−0.0845 (1)
O-2	0.4144 (1)	0.9031 (2)	0.1096 (1)
O-3	0.1048 (2)	1.5036 (4)	−0.1410 (2)
O-4	0.3961 (1)	0.6389 (2)	0.1619 (1)
C-1	0.1484 (1)	1.2564 (3)	−0.0196 (2)
C-2	0.1274 (2)	1.3017 (4)	0.0623 (2)
C-3	0.2124 (2)	1.2724 (4)	0.1353 (2)
C-4	0.2493 (1)	1.0903 (4)	0.1307 (1)
C-5	0.2755 (1)	1.0594 (3)	0.0504 (1)
C-6	0.3281 (1)	0.8922 (3)	0.0451 (1)
C-7	0.3537 (1)	0.8716 (3)	−0.0380 (1)
C-8	0.2691 (2)	0.8927 (3)	−0.1115 (1)
C-9	0.2185 (2)	1.0606 (4)	−0.1052 (1)
C-10	0.1885 (1)	1.0749 (3)	−0.0242 (1)
C-11	0.4077 (1)	0.7045 (3)	−0.0422 (1)
C-12	0.4510 (2)	0.7074 (4)	−0.1156 (2)
C-13	0.3527 (2)	0.5357 (4)	−0.0443 (2)
C-14	0.1192 (2)	0.9304 (4)	−0.0206 (2)
C-15	0.2514 (2)	0.9724 (4)	0.1890 (2)
C-16	0.0510 (2)	1.3911 (4)	−0.1414 (2)
C-17	−0.0377 (2)	1.3723 (5)	−0.2048 (2)
C-18	0.4428 (2)	0.7646 (3)	0.1590 (1)
C-19	0.5391 (2)	0.7879 (4)	0.2084 (1)

Voleneol Diacetate. Acetylation with acetic anhydride and pyridine yielded a monoacetate after 1 hr and a diacetate after 24 h. Crystallization from ether gave a quantitative yield of voleneol diacetate, mp 99.5–100.5 °C; mass spectrum m/e 322 (M^+), 262, 202 (base), 187, and 159; ^{1}H NMR δ 5.1 (br t, J = 10 Hz, 1 H), 4.8 (s, 1 H), 4.7 (dd, J = 5, 10 Hz, 1 H), 4.6 (s, 1 H), 2.1 (s, 3 H), 2.0 (s, 3 H), 0.91 (d, J = 6 Hz, 3 H), 0.86 (d, J = 6 Hz, 3 H), 0.73 (s, 3 H), 2.3–1.2 (11 H).

Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.81; H, 9.32. Found: C, 70.87; H, 9.26.

Crystallographic Study of Voleneol Diacetate (I). Colorless cyrstals were grown from ether. A needle 0.2 × 0.3 × 0.4 mm was mounted with the b axis parallel to the goniostat ϕ axis. The space group was determined to be $P2_1/c$. A Syntex four circle computer controlled diffractometer ($P2_1$) with a graphite monochrometer (MoK_α, λ 0.71069 Å) and pulse-height analyzer was used for collection of intensities. The cell constants, determined by least-squares treatment of 15 reflections, were a = 15.139 (9), b = 7.596 (4), c = 16.581 (9), β = 105.0°, ρ_{obsd} = 1.15 g/cm^3 (aq KI; ρ_{calcd} 1.13 g/cm^3), and Z = 4. The θ–2θ scan technique was employed at variable scan rate 0.5–29.3°/min (in 2θ). The scan range was 2.0°. The background to scan time ratio was 1.0. A total of 3587 reflections with $2\theta < 50°$ was collected and $2390 > 3\sigma$ (I) were considered observed. There were no significant variations in the intensities of three check reflections that were monitored after every 100 reflections. Standard deviations were assigned as described by Corfield et al.,[4] the value of p being 0.02. The intensities were corrected for Lorentz and polarization effects.

Phases for reflections with normalized structure factor $E > 1.5$ were

generated using the direct method program MULTAN.[5] All nonhydrogen atoms were located on the first E map. Full matrix least-squares refinement of positional and isotropic thermal parameters of nonhydrogen atoms reduced R to 0.184. Anisotropic refinement brought R down to 0.065. A difference map at this stage revealed all the hydrogens and two more cycles of refinement (anisotropic for nonhydrogens and isotropic for hydrogens) brought R down to the final value of 0.053. The refinement was based on F_0, the quantity minimized being $\Sigma w(F_o - F_c)^2$. The scattering factors used were those of Hanson et al.[6] No correction was applied for extinction.

Voleneol Monoacetate. Hydrolysis of voleneol diacetate (I) with $KHCO_3$ in methanol yielded a monoacetate after crystallization from ether: mp 89–90 °C; ^{1}H NMR δ 3.43 (dd, J = 5, 10 Hz, 1 H) and 2.0 (s, 3 H). The rest of the spectrum was similar to the diacetate with peaks at δ 4.7 and 2.1 absent.

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Registry No.—1, 64784-78-7; 1 monoacetate, 64784-79-8.

Supplementary Material Available: Tables of atomic coordinates of hydrogen atoms, temperature factors, bond distances, bond angles, and torsion angles, and packing diagram (6 pages). Ordering information is given on any current masthead page.

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Synthesis and Chemistry of Ethyl 2-Diethylphosphonoacrylate

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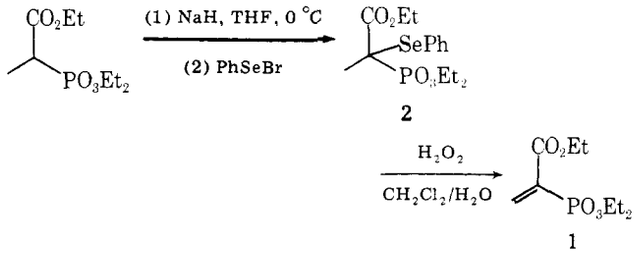
In recent years, vinyl phosphonium salts have found wide applicability in organic synthesis.[1] To date, numerous examples have been provided which demonstrate the utility of these reagents in the synthesis of acyclic,[1a] carbocyclic,[1b,f] and heterocyclic molecules[1c-e] containing carbon–carbon double bonds.

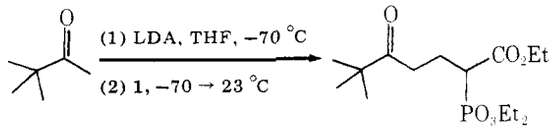
In contrast to the field of vinyl phosphonium salt chemistry, little attention has been given to the study of the synthesis and chemistry of vinyl phosphonates. Although reports of the synthesis of a few vinyl phosphonates have appeared in the literature,[2] the synthetic utility of these reagents has not been explored. Herein we describe a new synthesis of ethyl 2-diethylphosphonoacrylate (1)[2b] and reactions of this compound with a variety of anionic nucleophiles to produce stabilized phosphonate anions capable of undergoing subsequent reaction with aldehydes and ketones to produce unsaturated esters.

We chose to explore the possibility of using a selenoxide elimination as the method for generating the base-sensitive



unsaturation in **1**, due to the mildness of the reaction conditions necessary to achieve this transformation.[3] In fact, reaction of ethyl 2-diethylphosphonopropionate with sodium hydride followed by treatment with phenylselenyl bromide affords the selenylated derivative **2**, which is used without purification in the subsequent oxidation and elimination to give vinyl phosphonate **1** in an overall yield of 82%.

When vinyl phosphonate **1** is added slowly to a solution of the lithium enolate of pinacolone generated at −70 °C with lithium diisopropylamide (LDA) followed by slow warming to room temperature, keto ester phosphonate **3** is obtained in



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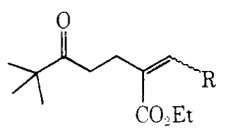
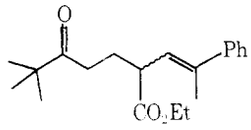
70% yield. If after warming to room temperature the intermediate phosphonate anion is allowed to react with an aldehyde or a ketone at reflux, unsaturated esters are isolated in good yield. Thus, reactions with benzaldehyde, propionaldehyde, 2-phenylpropionaldehyde, and cyclohexanone produce unsaturated esters **4, 5, 6** and **7** (~4:1 ratio), and **8** and **9** (~1:1 ratio) in 70, 78, 80, and 54% yields, respectively. We



4, R = Ph
5, R = CH_2CH_3
6, R = $CH(CH_3)Ph$



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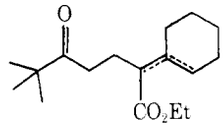

8, α,β isomer
9, β,γ isomer

were unable to obtain any appreciable yield of α,β-unsaturated ester in attempts to react the intermediate phosphonate anion with pivalaldehyde.

Similarly, reaction of the lithium enolates of 3-pentanone and *tert*-butyl acetate with vinyl phosphonate **1** followed by treatment of the resulting phosphonate anion with benzaldehyde at reflux furnishes α,β-unsaturated esters **10** and **11** in 74 and 69% yields, respectively. Treatment of the lithiated derivative of 1,3-dithiane[4] under analogous conditions affords α,β-unsaturated ester **12** in about 40% yield. All attempts to perform the analogous reaction using a 2-substituted 1,3-dithiane (i.e., 2-ethyl-1,3-dithiane) were uniformly unsuccessful.

Unsaturated esters **4, 5, 6, 7, 10, 11,** and **12** were isolated as a mixture of stereoisomers. The approximate ratios of these isomers were determined by integration of the appropriate vinyl proton resonances and (where necessary) by a comparison of the intensities of the characteristic resonances corre-

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