The ^{19}F NMR consisted of a doublet (from the CF_3 groups) centered at −13.8 ppm from an external trifluoroacetic acid reference. The coupling constant, J_{FF}, was 15.9 Hz. The signal from the fluorine on the center carbon atom would be expected to be a doublet of two 19 line multiplets, split by the hydrogen and the CF_3 groups, respectively, but was of too low an intensity to be observed. The ^1H NMR spectrum consisted of a doublet centered at τ 4.34. The coupling constant, J_{FH}, was 36.6 Hz. The gas-phase infrared spectrum contained bands at (cm^{-1}) 1440 (w), 1365 (m), 1300 (vs), 1290 (vs), 1265 (s), 1225 (w), 1195 (m), 1165 (w), 1080 (w), 1045 (s), 995 (s), 975 (w), 795 (w), 775 (m), 745 (m), 715 (m). The mass spectrum at 70 eV contained no peaks above m/e 381($C_8F_{15}^+$). The melting point was between −33 and −34 °C.

Perfluoro-2,2,4,4-tetramethylpentane. Anal. Calcd: C, 22.13; F, 77.87. Found: C, 22.58; F, 77.63. The ^{19}F NMR spectrum consisted of triplet (from the CF_3 groups) centered at −17.1 ppm from an external trifluoroacetic acid reference. The coupling constant, J_{FF}, was 14.9 Hz. The signal from the two fluorines on the center carbon atom would be expected to be a 19-line multiplet, but was of too low intensity to be observed. The gas-phase infrared spectrum contained bands at (cm^{-1}) 1300 (vs), 1285 (vs), 1270 (s), 1235 (w), 1195 (s), 1175 (w), 1150 (w), 1095 (w), 1025 (w), 990 (s), 815 (m), 750 (m), 740 (s), 715 (m). The mass spectrum at 70 eV contained a peak at m/e 469, assigned to the parent minus fluorine. The melting point was between −24 and −25 °C.

Fluorination of 3,3-Dihydrooctadecafluoro-2,2,4,4-tetramethylpentane. The fluorination system was flushed with helium for 12 h, and then the first two zones of the reactor were cooled to −78 °C and 0.5 g of 3,3-dihydrooctadecafluoro-2,2,4,4-tetramethylpentane was injected. The helium flow was terminated and the fluorine flow was set to 1.5 cm^3/min. After 24 h, reactor zones 3 and 4 were cooled to −78 °C and the first two zones were warmed to room temperature. After an additional 48 h, the reaction was terminated and the product was collected. The product was found to consist entirely of the starting material.

Registry No.—2,2,4,4-Tetramethylpentane, 1070-87-7; 3,3-dihydrooctadecafluoro-2,2,4,4-tetramethylpentane, 41296-82-6; 3-hydrononadecafluoro-2,2,4,4-tetramethylpentane, 62375-53-5; perfluoro-2,2,4,4-pentamethylpentane, 62375-54-6.

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Conversion of Virescenol A into Virescenol B

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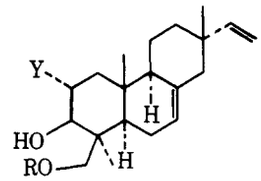
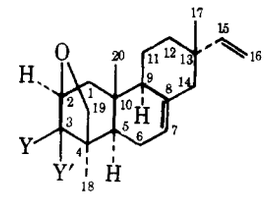
In connection with a study of the chemistry of virescenol A (**1a**), the aglycone of several of the fungal, virescenoside metabolites,[1] the tetrahydrofuran **2a** has been encountered frequently and now has been utilized for the conversion of virescenol A into B (**1b**).[2]

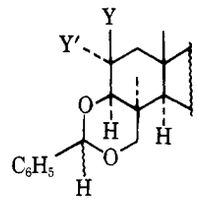
Treatment of virescenol A (**1a**) with benzaldehyde and zinc chloride yielded the benzylidene derivative **3a**,[3] whose reduction with lithium aluminum hydride in the presence of aluminum chloride led to ether **1e**. Attempted tosylation of the latter in pyridine solution gave the hydroxy ether **2a**, presumably by sequential formation of **1f** and the oxonium salt **4**, followed by pyridine debenzylation of the latter.



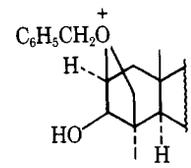
1a, R = H; Y = OH
b, R = Y = H
c, R = Ts; Y = OH
d, R = Ts; Y = OTs
e, R = $CH_2C_6H_5$; Y = OH
f, R = $CH_2C_6H_5$; Y = OTs
g, R = H; Y = OTs



2a, Y = OH; Y′ = H
b, Y + Y′ = O
c, Y = H; Y′ = OH



3a, Y = H; Y′ = OH
b, Y + Y′ = O
c, Y = OH; Y′ = H



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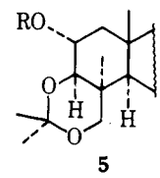

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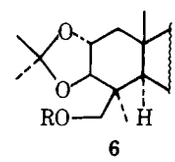

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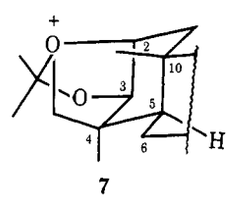
a, R = H
b, R = Ts

Treatment of virescenol A (**1a**) with acetone and cupric sulfate produced the isopropylidene derivatives **5a**[4] and **6a**, whose tosylation afforded sulfonic esters **5b** and **6b**, respectively. Even though the latter was stable, tosylate **5b** was converted into the ether **2a** on standing or on exposure to silica gel in benzene. This transformation may be the consequence of displacement of the tosylate by a ketal oxygen (cf. **7**), followed by hydrolysis, or prior hydrolytic formation of dihydroxytosylate **1g** and subsequent internal displacement.



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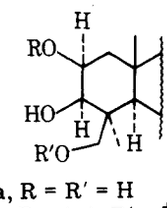
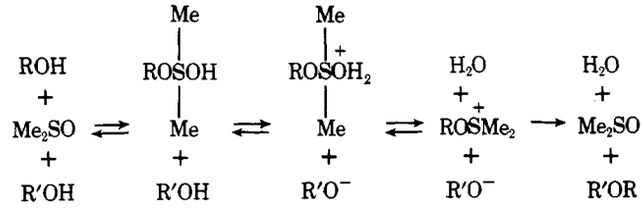


8a, R = R′ = H
b, R = (−); R′ = $^+SMe_2$

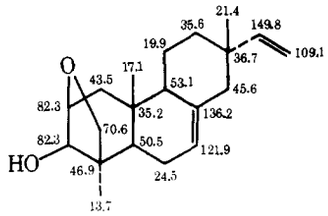
Collins oxidation of the hydroxy acetal **3a** and sodium borohydride reduction of the resultant ketone **3b** gave the isomeric hydroxy acetal **3c**, whose acid hydrolysis yielded 2-



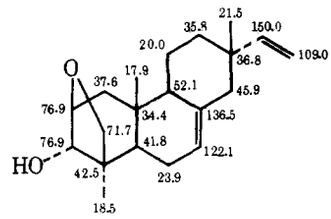
epivirescenol A (**8a**). In analogy with previous reports of tetrahydrofuran formation,[5] heating of a dimethyl sulfoxide solution of **8a** led to a high yield of hydroxy ether **2a**, presumably by way of the mechanism below and hence via intermediate **8b**. Even thermolysis of virescenol A (**1a**) itself in dimethyl sulfoxide produced **2a**, albeit in low yield.

Collins oxidation of hydroxy ether **2a**, thus prepared by a variety of paths from virescenol A (**1a**) (vide supra), yielded ketone **2b**, whose reduction in liquid ammonia with lithium and ethanol yielded virescenol B (**1b**) along with tetrahydrofurans **2a** and **2c**. The latter was also the product of sodium borohydride reduction of ketone **2b** in analogy with the stereoselective hydride reductions of bicyclo[3.2.1]octan-8-ones.[6] The C(3) stereochemistry of the two hydroxytetrahydrofurans was confirmed by ^{13}C NMR spectroscopy.

The carbon shifts of **2a** and **2c** are based on those of isopimaradiene[7] and virescenol B (**1b**)[8] and are listed on formulas **9** and **10**, respectively. The strong shielding of C(1) and C(5)



9



10

in **2c** (**10**) indicates the ring A axiality of the 3-hydroxy group in this isomer. Similarly, the shielding of the 4-methyl group in **2a** reveals a closer proximity of the methyl function to its neighboring hydroxy group in **2a** than in **2c**. These facts confirm the ring A stereochemistry of the two isomeric alcohols.

Experimental Section

Melting points were determined on a Reichert micro hotstage and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer 167 spectrophotometer. ^1H NMR spectra of $CDCl_3$ and CCl_4 solutions (Me_4Si, $\delta = 0$) were recorded on a Jeol H-60 spectrometer, while the ^{13}C NMR spectra were produced on a Varian XL-100-15 spectrometer operating at 25.2 MHz in the Fourier transform mode.

3-*O*,19-*O*-Benzylidenevirescenol A (3a). A mixture of benzaldehyde (16 g), zinc chloride (4.0 g), and virescenol A (3.2 g) was stirred at room temperature for 12 h. It then was poured into ice water and extracted with chloroform. The extract was washed in water, dried (Na_2SO_4), and concentrated and the excess benzaldehyde (13 g) was removed by distillation. Chromatography of the residue (6.4 g) on silica and elution with petroleum ether yielded benzaldehyde (1.5 g). Continued elution with 1:1 petroleum ether/ether gave 2.8 g (65%) of **3a**: mp 172–174 °C (methanol); IR ($CHCl_3$) 3580 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.86, 1.03, 1.48 (s, 9, Me_3), 3.40 (d, 1, J = 10 Hz, H-3), 3.63, 4.23 (dd, 2, J = 11 Hz, H-19), 4.46 (m, 1, H-2), 5.70 (s, 1, benzyl H), 7.1–7.6 (m, 5, aromatic Hs).

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.24; H, 8.96.

19-*O*-Benzylvirescenol A (1e). A solution of 0.15 g of **3a** in 10 mL of anhydrous tetrahydrofuran was added dropwise to a stirring suspension of 0.12 g of lithium aluminum hydride and 0.20 g of aluminum chloride in 10 mL of tetrahydrofuran under nitrogen and the mixture refluxed for 3 h. $Na_2SO_4 \cdot 10H_2O$ was added cautiously; the mixture was shaken and then filtered. Evaporation of the filtrate gave a residue (0.14 g) which was chromatographed on silica. Elution with 9:1 benzene/ethyl acetate gave 0.10 g (67%) of oily diol **1e**: IR ($CHCl_3$) 3560 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.86, 0.90, 1.30 (s, 9, Me_3), 3.04 (d, 1, J = 10 Hz, H-3), 3.42, 3.98 (dd, 2, J = 10 Hz, H-19), 3.69 (m, 1, H-2), 4.48 (s, 2, benzyl H), 7.3 (m, 5 H, aromatic Hs).

Anal. Calcd for $C_{27}H_{38}O_3$: C, 78.98; H, 9.33. Found: C, 78.74; H, 9.25.

2β,19-*O*-Dehydrovirescenol B (2a). A solution of 0.9 g of **1e** and 0.6 g of tosyl chloride in 10 mL of pyridine was stirred at room temperature for 48 h. It then was poured into ice water and extracted with chloroform. The extract was washed with 1 N hydrochloric acid and water, dried, and concentrated. Chromatography of the residue (1.1 g) on silica and elution with 99:1 chloroform/methanol gave 0.3 g (45%) of **2a**: mp 166–168 °C; IR (CCl_4) 3610 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.88, 1.02, 1.12 (s, 9, Me_3), 3.51 (s, 1, H-3), 3.45, 3.97 (dd, 2, J = 9 Hz, H-19), 4.17 (m, 1, H-2).

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.22; H, 10.15.

Isopropylidene Derivatives of Virescenol A (5a and 6a). A mixture of **1a** (0.45 g) and copper sulfate (1.1 g) in 15 mL of acetone was stirred at room temperature for 3 h. It then was filtered and evaporated, and the residue (0.55 g) was chromatographed on Florisil. Elution with benzene gave a fraction (0.15 g, 28%) whose crystallization from methanol yielded **6a**: mp 173–175 °C; IR ($CHCl_3$) 3545 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.85, 0.93, 1.23, 1.43, 1.46 (s, 15, Me_5), 3.16 (d, 1, J = 10 Hz, H-3), 3.33, 4.13 (dd, 2, J = 11 Hz, H-19), 3.80 (m, 1, H-2).

Anal. Calcd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.38; H, 10.25.

Continued elution with 9:1 benzene/ethyl acetate gave 0.15 g (28%) of oily **5a**: IR ($CHCl_3$) 3560 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.86, 0.96, 1.33, 1.43, 1.53 (s, 15, Me_5), 3.16 (d, 1, J = 10 Hz, H-3), 3.33, 4.13, (dd, 2, J = 12 Hz, H-19), 4.16 (m, 1, H-2).

Anal. Calcd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.50; H, 10.35.

Further eluction with 4:1 benzene/ethyl acetate gave 0.14 g of starting triol **1a**.

3-*O*,19-*O*-Isopropylidenevirescenol A Tosylate (5b). A solution of 0.20 g of **5a** and 0.15 g of tosyl chloride in 5 mL of pyridine was stirred at room temperature for 48 h. It then was poured into ice water and extracted with chloroform. The extract was washed with 1 N hydrochloric acid and water, dried, and concentrated. Chromatography of the residue (0.3 g) on silica and elution with benzene gave 0.22 g (73%) of oily **5b**: NMR ($CDCl_3$) δ 0.81, 1.00 (s, 6, Me_2), 1.23 (s, 9, Me_3), 2.40 (s, 3, aromatic Me), 3.13 (d, 1, J = 16 Hz, H-3), 3.33, 3.93 (dd, 2, J = 11 Hz, H-19), 4.93 (m, 1, H-2), 7.1, 7.8 (dd, 4, J = 10 Hz, aromatic Hs).

Anal. Calcd for $C_{30}H_{42}O_5S$: C, 70.01; H, 8.23. Found: C, 70.32; H, 8.02.

A mixture of **5b** (0.1 g) and silica gel (1.0 g) in benzene (5 mL) was stirred at room temperature for 2 h. It was filtered and the filtrate concentrated under vacuum. The residue (80 mg) was chromatographed on silica and elution with 9:1 benzene/ethyl acetate gave pure **2a** (vide supra).

2-*O*,3-*O*-Isopropylidenevirescenol A Tosylate (6b). The same treatment of 0.2 g of **6a** and workup gave 0.2 g (70%) of oily **6b**: NMR ($CDCl_3$) δ 0.86, 0.90, 1.13, 1.33, 1.36 (s, 15, Me_5), 2.43 (s, 3, aromatic Me), 3.06 (d, 1, J = 10 Hz, H-3), 3.52 (m, 1, H-2), 4.20 (br s, 2, H-19), 7.15, 7.85 (dd, 4, J = 10 Hz, aromatic Hs).

Anal. Calcd for $C_{30}H_{42}O_5S$: C, 70.01; H, 8.23. Found: C, 70.20; H, 8.07.

Keto Ketal 3b. A solution of **3a** (0.3 g) in methylene chloride (5 mL) was added dropwise (15 min) to a suspension of Collins reagent (1.0 g) in anhydrous methylene chloride (15 mL) and the mixture was stirred at room temperature for 15 min. It was filtered and the filtrate was washed with 10% acetic acid solution. The combined organic solutions were washed with 5% sodium hydroxide, dried, and evaporated. Chromatography of the residue on silica and elution with chloroform gave 0.2 g (68%) of oily ketone **3b**: IR ($CHCl_3$) 1718 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.87, 1.00, 1.60 (s, 9, Me_3), 3.61, 4.15 (dd, 2, J = 11 Hz, H-19), 4.30 (s, 1, H-3), 5.97 (s, 1, benzyl H), 7.2–7.7 (m, 5 H, aromatic Hs).

Anal. Calcd for $C_{27}H_{34}O_3$: C, 79.76; H, 8.43. Found: C, 80.00; H, 8.20.

3-*O*,19-*O*-Benzylidene-2-epivirescenol A (3c). Sodium borohydride (85 mg) was added to a solution of **2b** (0.25 g) in tetrahydrofuran (15 mL) and the mixture was stirred at room temperature for 5 min. Then a 0.1 N sulfuric acid solution (50 mL) was added and the mixture was extracted with chloroform. The extract was washed with saturated sodium bicarbonate solution, dried, and concentrated under vacuum. The residue (0.2 g) was crystallized from 3:2 petroleum ether/benzene, giving 0.15 g (44%) of crystalline **3c**: mp 168–170 °C;

IR ($CHCl_3$) 3575 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.90, 1.16, 1.41 (s, 9, Me_3), 3.50 (d, 1, J = 3Hz, H-3), 3.58, 4.62 (dd, 2, J = 11 Hz, H-19), 6.49 (s, 1, benzyl H), 7.2–7.7 (m, 5 H, aromatic Hs).

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.50; H, 8.58.

2-Epivirescenol A (8a). A mixture of 0.25 g of **3c** and 5 mL of 0.1 N methanolic sulfuric acid in 5 mL of chloroform was refluxed for 5 h. It was diluted with water and extracted with chloroform. The extract was washed with water, dried, and concentrated under vacuum. Chromatography of the residue (90 mg) on silica and elution with 6:1 benzene/ethyl acetate gave 0.13 g (65%) of a solid whose crystallization from 1:1 benzene/petroleum ether yielded crystalline **8a:** mp 168–170 °C; IR ($CHCl_3$) 3570 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.85, 1.05, 1.20 (s, 9, Me_3), 3.38 (m, 1, H-3), 3.48, 4.63 (dd, 2, J = 11 Hz, H-19).

Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.62; H, 10.30.

A solution of **8a** (0.20 g) in Me_2SO (5 mL) was stirred under nitrogen at 160 °C for 4 h. It then was poured into water and the mixture was extracted with chloroform. The extract was washed with water, dried, and concentrated under vacuum. Chromatography of the residue (0.16 g) on silica and elution with 6:1 benzene/ethyl acetate gave 0.14 g of **2a** (vide supra).

A solution of virescenol A (**1a**) (0.20 g) was treated in the same manner. The same workup gave 50 mg of **2a** (vide supra).

Keto Ether 2b. A solution of hydroxy ether **2a** (0.2 g) in methylene chloride (5 mL) was added dropwise (10–15 min) to a suspension of Collins reagent (0.7 g) in anhydrous methylene chloride (10 mL). The mixture was allowed to stir for an additional 15 min and filtered. The dark filtrate was washed successively with 1 N sulfuric acid and water and concentrated under vacuum. The light brown residue was purified by chromatography on silica. Elution with chloroform led to 0.2 g (100%) of oily **2b:** IR (CCl_4) 1762 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.91, 1.00, 1.30 (s, 9, Me_3), 3.78, 4.39 (dd, 2, J = 11 Hz, H-19), 4.04 (d, 1, J = 6 Hz, H-2).

Anal. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 80.15; H, 9.17.

Reduction of Keto Ether 2b. To a solution of **2b** (0.40 g) in methanol (20 mL) was added a solution of sodium borohydride (90 mg) in 6 mL of 50% aqueous methanol. The mixture was stirred at room temperature for 10 min and then 50 mL of 0.5 N sulfuric acid solution was added thereto. It was extracted with chloroform and the extract was washed with saturated sodium bicarbonate solution, dried, and concentrated under vacuum. Chromatography of the residue on silica and elution with 50:1 chloroform/methanol gave 0.38 g (94%) of oily **2c:** IR (CCl_4) 3650 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.83, 0.88, 1.04 (s, 9, Me_3), 3.36, 3.96 (dd, 2, J = 9.5 Hz, H-19), 3.76 (d, 1, J = 6 Hz, H-3), 4.10 (m, 1, H-2).

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.35; H, 9.85.

A solution of 0.16 g of ketone **2b** in 10 mL of 9:1 tetrahydrofuran/ethanol was added over a 10-min period to a solution of lithium (15 mg) in 30 mL of liquid ammonia and the reaction mixture was stirred at −40 °C for 10 min. A few drops of bromobenzene were added to the mixture, the ammonia was evaporated in a stream of nitrogen, and 20 mL of a 0.5 N sulfuric acid solution was added to the residue. The resulting mixture was extracted with chloroform and the extract combined, washed with water, dried, and concentrated under vacuum. Chromatography of the residue (0.12 g) on silica and elution with 9:1 benzene/ethyl acetate gave 25 mg of **2c** (vide supra). Elution with 6:1 benzene/ethyl acetate gave 35 mg of **2a** (vide supra) and 30 mg of virescenol B (**1b**), identical in all respects with an authentic sample.[1]

Tosylation of Virescenol A (1a). A solution of 0.96 g of **1a** and 0.70 g of tosyl chloride in 10 mL of pyridine was stirred at room temperature for 72 h. It was poured into ice water and extracted with chloroform. The extract was washed with 1 N hydrochloric acid and water, dried, and concentrated. Chromatography of the residue (1.2 g) on silica and elution with 9:1 benzene/ethyl acetate gave 0.25 g (13%) of virescenol A 2,19-ditosylate (**1d**) [IR ($CHCl_3$) 3540 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.86 (s, 6, Me_2), 1.03 (s, 3, Me), 2.43 (s, 6, aromatic Me_2), 3.26 (d, 1, J = 10 Hz, H-3), 3.96 (s, 2, H-19), 4.73 (m, 1, H-2), 7.1–7.8 (m, 8, aromatic Hs)], 0.18 g (19%) of tetrahydrofuran **2a** (vide supra), and 0.40 g (28%) of virescenol A 19-tosylate (**1c**) [IR ($CHCl_3$) 3575 cm^{-1} (OH); NMR (CCl_4) δ 0.84 (s, 6, Me_2), 1.50 (s, 3, Me), 2.38 (s, 3, aromatic Me), 7.3–7.6 (dd, 4 H, J = 8 Hz, aromatic Hs)].

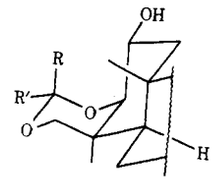
Registry No.—**1a,** 22343-46-9; **1b,** 22343-47-1; **1c,** 63089-00-9; **1d,** 63089-01-0; **1e,** 63089-02-1; **2a,** 63089-03-2; **2b,** 63089-04-3; **2c,** 63121-82-4; **3a,** 63089-05-4; **3b,** 63089-06-5; **5a,** 63089-07-6; **5b,** 63089-08-7; **6a,** 63089-09-8; **6b,** 63089-10-1; **8a,** 63089-11-2; benzaldehyde, 100-52-7.

References and Notes

(1) N. Cagnoli Bellavita, P. Ceccherelli, M. Ribaldi, J. Polonsky, and Z. Baskevitch, *Gazz. Chim. Ital.*, **99**, 1354 (1969); P. Ceccherelli, N. Cagnoli Bellavita, J. Polonsky, and Z. Baskevitch, *Tetrahedron*, **29**, 449 (1973).

(2) The $\Delta^{8(9)}$ isomer of **2a** has been shown previously to accompany the tosylates $\Delta^{8(9)}$-**1c** and $\Delta^{8(9)}$-**1d** as a product of the derivatization of isovirescenol A ($\Delta^{8(9)}$-**1a**) [J. Polonsky, Z. Baskevitch, N. Cagnoli Bellavita, and P. Ceccherelli, *Bull. Soc. Chim. Fr.*, 1912 (1970)].

(3) This substance probably possesses the benzylic β-hydrogen configuration, depicted in conformational structure i.



i, R = H; R′ = C_6H_5
ii, R = R′ = Me

(4) This ketal can be represented by structure ii, in which an energetically unfavorable, 1,3-diaxial, nonbonded interaction exists between the ketal β-methyl group and the C(2)–C(3) bond. This may be responsible for the production of two ketals, but only one acetal.

(5) B. T. Gillis and P. E. Beck, *J. Org. Chem.*, **28**, 1388 (1963); P. R. Jefferies and C. A. Henrick, *Chem. Ind. (London)*, 1801 (1963).

(6) E. Wenkert and Z. Kumazawa, *Chem. Commun.*, 140 (1968).

One-Vessel Synthesis of 4-Hydroxyproline from Glyoxal and Oxaloacetic Acid[1]

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4-Hydroxyproline, obtained initially by isolation from gelatin hydrolyzates,[2] was first synthesized by Leuchs,[3] and subsequently by a variety of other procedures. Some of these were variants of the Leuchs method involving a valerolactone intermediate;[4–8] others were based on different routes,[9–12] but generally required rather complex reaction sequences, commercially unavailable starting materials, or necessitated the isolation of intermediates.

We report here a new synthesis of the mixed racemates of 4-hydroxyproline, obtained in good yield from the commercially available starting compounds, glyoxal and oxaloacetic acid. Although this procedure was briefly cited earlier[13] in connection with the use of one of the intermediates (**3,** Scheme I), no details were presented. The entire reaction sequence is carried out in a single vessel, the yield is approximately 40% (mixture of racemates), and the starting materials have the advantage that at least one can be obtained readily in radioactive form,[14] since the goal in synthesizing 4-hydroxyproline is usually to obtain the radioactive (especially, the ^{14}C) product.

Results and Discussion

In outline, this procedure involves simply the reaction of equimolar glyoxal and oxaloacetic acid in aqueous solution at room temperature and neutral pH, and the subsequent addition, successively, of excess NH_4OH and sodium borohydride. Our speculation concerning intermediate steps is outlined in Scheme I, as supported by previous reports of analogous synthetic steps, involving the condensation of glyoxylic acid and oxaloacetic acid to form 4-hydroxy-2-ketoglutaric acid[15,16] (in analogy with **3,** Scheme I), the formation of pyrrole-2-carboxylic acid[17] (in analogy with **6,** Scheme I),