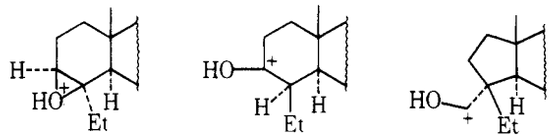
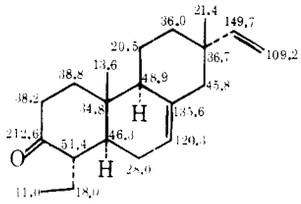


6 7 8

ketone (7), whose enolization and reketonization gives ketone **2a**, whereas C(2)–C(3) bond migration to C(4) of **6** yields the conjugate acid (8) of aldehyde **3a**.

The carbon shifts of ketone **2a** are outlined on formula **9**. The similarity of the C(2) shift of 38.2 ppm with that of 5α-androstan-3-one (38.1 ppm)[6] shows the ethyl group to be equatorial and hence 4α oriented. The assignment of the chemical shifts of the alcohols **2b** and **2c** is portrayed on formulas **10** and **11**, respectively.



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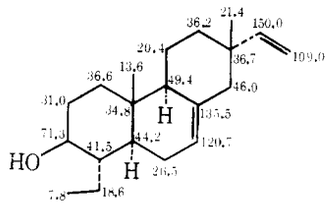

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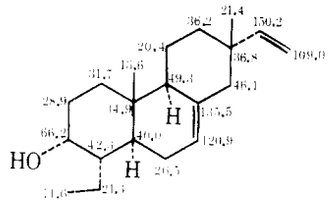

11

The migration of C(18) from C(4) to C(19) in the solvolysis of virescenol B 19-tosylate (**1b**) may be of biogenetic significance. Whereas many one-carbon rearrangements abound in the pimaranic diterpene field, none of the aforementioned type has been observed heretofore. Nevertheless, an ethano unit attachment to C(4) of diterpene rings A, such as in ketone **2a**, appears in the form of a furan ring in some constituents of the coffee bean.[10]

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 (Me_4Si, $\delta = 0$) were recorded on a Jeol H-60 spectrometer and the ^{13}C NMR spectra were produced on a Varian XL-100-15 spectrometer operating at 25.2 MHz in the Fourier transform mode.

Solvolysis of Virescenol B Tosylate (1b). A solution of 600 mg of tosylate **1b** in 7 mL of dimethyl sulfoxide was heated at 95 °C under nitrogen with stirring for 7 h. After the addition of 50 mL of saturated brine solution the mixture was extracted thoroughly with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated under vacuum. Chromatography of the residual oil, 330 mg, on silica gel and elution with benzene yielded 60 mg (16%) of liquid aldehyde **3a:** IR (CCl_4) 2670 (CHO), 1722 (C=O) cm^{-1}; NMR (C_6D_6) δ 0.68, 0.86 (s, 3 each, Me_2), 0.73 (t, 3, J = 6 Hz, Me of Et), 8.96 (s, 1, CHO).

Anal. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.70; H, 10.72.

Elution with 20:1 benzene–ethyl acetate gave 185 mg (50%) of solid whose crystallization from pentane led to crystalline ketone **2a:** mp 92–94 °C; IR (CCl_4) 1708 cm^{-1} (C=O); NMR (C_6D_6) δ 0.76, 0.90 (s, 3 each, Me_2), 0.96 (t, 3, J = 6 Hz, Me of Et).

Anal. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.92; H, 10.54.

Alcohols 2b and 2c. A solution of 60 mg of sodium borohydride in 5 mL of ethanol was added dropwise to a stirring solution of 600 mg of ketone **2a** in 15 mL of ethanol at 0 °C. The mixture then was stirred at room temperature for 1 h and poured into ice water. It was extracted with chloroform and the extract dried (Na_2SO_4) and evaporated. Chromatography of the oily residue, 550 mg, on silica gel and elution with 20:1 benzene–ethyl acetate afforded 180 mg (30%) of semisolid alcohol **2c:** IR (CCl_4) 3625 cm^{-1}(OH); NMR (CCl_4) δ 3.86 (m, 1 OCH).

Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.42; H, 11.02.

Further elution with the same solvent pair gave 310 mg (51%) of solid whose crystallization from pentane–benzene yielded crystalline alcohol **2b:** mp 120–125 °C; IR (CCl_4) 3620 cm^{-1}(OH); NMR (CCl_4) δ 3.20 (m, 1, OCH).

Anal. Calcd. for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.38; H, 11.00.

Alcohol 3b. A solution of 15 mg of sodium borohydride in 5 mL of ethanol was added dropwise to a stirring solution of 50 mg of aldehyde **3a** in 3 mL of ethanol at 0 °C. The mixture then was stirred at room temperature for 1 h. Workup as above, chromatography of the curde product, 40 mg, on silica gel, and elution with 30:1 benzene–ethyl acetate led to 35 mg (80%) of semisolid alcohol **3b:** NMR δ 3.25, 3.45 (AB dd, 2, J = 11 Hz, OCH_2).

Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.05; H, 11.31.

Acknowledgment. P.C. and M.C. acknowledge with thanks financial support by the Consiglio Nazionale delle Ricerche (C.N.R.). The authors are grateful to Professor N. Cagnoli-Bellavita for her interest in this study.

Registry No.—**1b,** 67393-59-3; **2a,** 67393-60-6; **2b,** 67393-61-7; **2c,** 67393-62-8; **3a,** 67393-63-9; **3b,** 67393-64-0.

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Novel Applications of the Potassium Chlorate–Osmium Tetroxide Oxidizing System. Synthesis of α-Dicarbonyl Derivatives from Acetylenic Compounds. Synthesis of a 2,3-Dihydroxy-1,4-dione from a 2,5-Dialkylfuran

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The cis hydroxylation of olefins to α-diols by metal chlorates in aqueous solution containing catalytic amounts of osmium tetroxide has found wide use.[1] This method is especially useful when the oxidation of other organic functions present in the substrate has to be avoided; most of these functions are, in fact, unaffected by the said oxidizing system. The reaction of acetylenic compounds with this oxidizing

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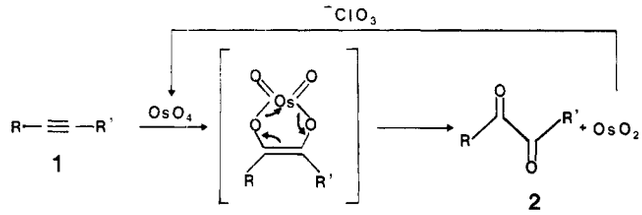
mixture has, however, never been reported previously in the literature. Being interested in the preparation of some α-dicarbonyl compounds, we speculated that the said oxidation may afford the desired derivatives in one step from the corresponding acetylenic precursors. A plausible mechanism for this reaction is, in fact, as follows.[2]



a: R = Me ; R' = OMe

b: R = Et ; R' = OMe

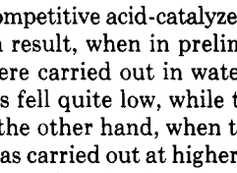
c: R = i-Pr ; R' = OMe

d: R = R' = CH_3CH(OH)

The present paper reports the successful application of this reaction (potassium chlorate was used for the in situ osmium tetroxide regeneration) for the preparation of α-keto acid methyl esters **2a–c** and 2,5-dihydroxyhexane-3,4-dione (**2d**; existing only as the polymeric form[3]) from 1-methoxy-1-alkynes **1a–c** and 3-hexyne-2,5-diol (**1d**), respectively. Our interest for these synthesis relyed in the fact that α-keto esters can be converted[4] to optically active α-amino acids by asymmetric synthesis and that **2c** affords,[3] by acid-catalyzed cyclization, 2,5-dimethyl-4-hydroxy-2,3-dihydrofuran-3-one (furaneol), a flavor principle of pineapple and strawberry whose preparation has become of substantial practical interest.[5]

In the reaction of the acetylenic derivatives **1** with the aqueous potassium chlorate–osmium tetroxide mixture, the development of slight acidity (final pH, ~3.5–5.0) from side reactions occurred and caused with substrates of type **1a–c**, but not with **1d**, competitive acid-catalyzed hydratation of the triple bond.[6] As a result, when in preliminary experiments these reactions were carried out in water at "free" pH, the α-keto ester yields fell quite low, while the yield for **2d** was high (~85%). On the other hand, when the reaction on type **1a–c** substrates was carried out at higher pH values (with **1a** and **1c** a series of experiments at constant pH 5.4, 5.9, 6.4, or 6.8 was performed[7]), the rate of oxidation to α-keto ester decreased so much as to allow the addition of hypochlorous acid to the triple bond[8] to become the predominant reaction. Finally, when the reaction was performed in a water–ether mixture at "free" pH, satisfactory yields of α-keto esters **2a–c** from **1a–c** could be achieved (48, 69, and 80%, respectively). In such a system, in fact, due to the low solubility of the acetylenic ethers **1a–c** in the aqueous phase, the addition of water, as well as that of hypochlorous acid, to the triple bond is depressed considerably, while the reaction between substrate and osmium tetroxide can take place in the ether phase, where both of the latter are freely soluble.

Another known direct precursor of furaneol (base-catalyzed cyclization) is *erythro*-3,4-dihydroxyhexane-2,5-dione[9] (**5**), which has been prepared previously by bromination of 2,5-dimethylfuran (**4**) in methanol solution to 2,5-dimethyl-2,5-dimethoxy-2,5-dihydrofuran (**3**) (60% yield),[10] followed by oxidation of the latter with potassium chlorate and a catalytic amount of osmium tetroxide in aqueous tetrahydrofuran (~100% yield of crude **5**).[9] It occurred to us, however, that this system might oxidize **4** directly to the dihydroxyhexanedione level. In fact, we have now found that this synthesis too can be realized and that the product of the reaction, carried out in water, is the erythro isomer **5** (61% yield).



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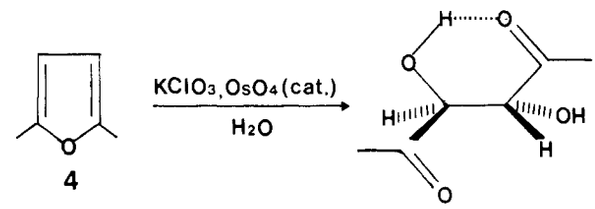

4 **5** (erythro isomer)

To our knowledge this reaction represents the first example of oxidation with a metal chlorate–osmium tetroxide mixture of a 2,5-dialkylfuran to a 2,3-dihydroxy-1,4-dione.

Experimental Section

Materials. Osmium tetroxide was from Merck, and 3-hexyne-2,5-diol and 2,5-dimethylfuran were purchased from Fluka. The 1-methoxy-1-alkynes (RC≡COMe) were prepared according to Nooi and Arens[11] from the corresponding aldehydes (RCH_2CHO). The latter and all other materials were obtained from Carlo Erba.

Spectra. The IR spectra were taken with a Perkin-Elmer 457 spectrometer and the 60 MHz ^1H NMR spectra with a Varian T-60 instrument using tetramethylsilane as an internal standard.

General Procedure for the Preparation of α-Keto Esters 2a–c. A mixture of 0.15 mol of 1-methoxy-1-alkyne (**1a–c**), 36.76 g (0.30 mol) of $KClO_3$, 1.52 g (6 mmol) of OsO_4 (*caution: vapor is poisonous!*), 200 mL of water, and 300 mL of ether was stirred at room temperature until the black coloring of the mixture disappeared. The organic phase was separated and the aqueous phase extracted with ether in a continuous extractor (~4 h). The combined ether solutions were dried (Na_2SO_4), the solvent was evaporated, together with the OsO_4, at 0 °C on a rotary evaporator, and the α-keto ester (**2a–c**) was distilled from the residue under vacuum through a Vigreux fractionating column.

2-Oxopropanoic Acid Methyl Ester (2a): reaction time, 4 h; bp 50–53 °C (15 mm) [lit.[12] bp 53 °C (15 mm)]; yield 48%; IR and ^1H NMR spectra were identical with those reported for **2a**.[13,14]

2-Oxobutanoic Acid Methyl Ester (2b): reaction time, ~16 h (overnight); bp 72–74 °C (27 mm) [lit.[15] bp 72–74 °C (27 mm)]; yield 69%; IR (film) 1730 cm^{-1}; ^1H NMR (C_6D_6) δ 0.90 (3 H, t, J = 6 Hz, CH_3C), 2.57 (2 H, q, J = 6 Hz, CH_2), 3.53 (3 H, s, $COOCH_3$).

3-Methyl-2-oxobutanoic Acid Methyl Ester (2c): reaction time, ~16 h (overnight); bp 64–68 °C (23 mm); yield 80%; IR (film) 1730 cm^{-1}; ^1H NMR (C_6D_6) δ 1.08 (6 H, d, J = 6 Hz, $(CH_3)_2C$), 3.15 (1 H, m, J = 6 Hz, CH), 3.42 (3 H, s, $COOCH_3$).

2,5-Dihydroxyhexane-3,4-dione (2d). A mixture of 1.14 g (10.0 mmol) of **1d**, 2.80 g (22.8 mmol) of $KClO_3$, and 0.050 g (0.197 mmol) of OsO_4 (*caution: vapor is poisonous!*) in 15 mL of water was stirred at room temperature for 18 h. The water was removed, together with the OsO_4, under vacuum (1 mm) at room temperature, and the residue was extracted at room temperature and under stirring with four successive 30-mL portions of acetone. The combined filtered extracts were dried (Na_2SO_4) and rotary evaporated at room temperature (until constant weight) to a yellow viscous residue of 1.23 g (84.5%) of **2d** (polymeric form[3]); IR and ^1H NMR spectra and TLC and VPC behavior were in accord with those reported in the literature for **2d**.[3] Cyclization of the above unpurified **2d** by a literature procedure[3] gave furaneol (50% overall yield from **1d**).

***erythro*-3,4-Dihydroxyhexane-2,5-dione (5).** The oxidation of 0.96 g (10.0 mmol) of **4** and workup were carried out as for substrate **1d**, the only differences being that ethyl acetate (4 × 30 mL) was used instead of acetone to extract the first residue and that the final residue was crystalline. The latter was recrystallized from chloroform–petroleum ether to give 0.89 g (61%) of pure **5**: mp 60–62 °C (lit.[9] mp 59–61 °C); IR, ^1H NMR, and mass spectra were identical with those reported in the literature for **5**.[9]

Registry No.—**1a**, 13169-01-2; **1b**, 13279-94-2; **1c**, 55755-14-1; **1d**, 3031-66-1; **2a**, 600-22-6; **2b**, 3952-66-7; **2c**, 3952-67-8; **4**, 625-86-5; **5**,

36871-95-1; potassium chlorate, 3811-04-9; osmium tetroxide, 20816-12-0.

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Aleuritic Acid, an Abundant Source of Prostanoid Synthons

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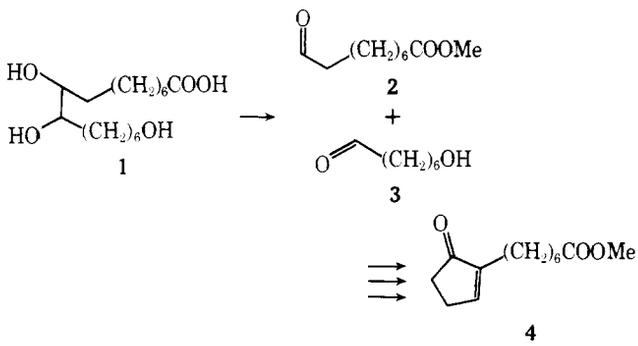
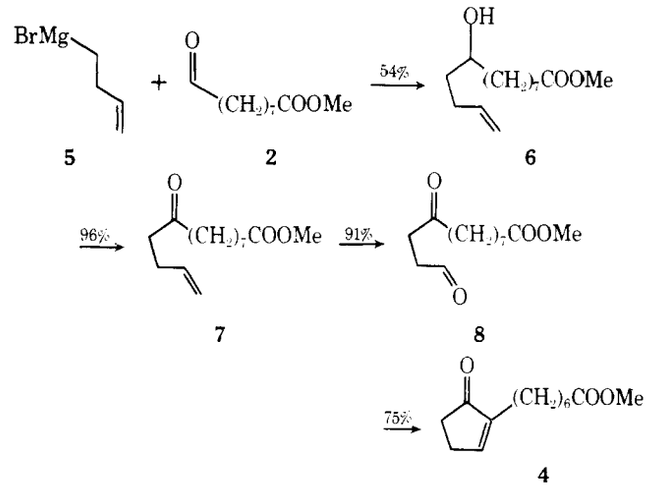
An attractive strategy for the construction of valuable prostanoids exploits readily available synthons derived from natural products.[1] Aleuritic acid (**1**) is a major component of shellac.[2,3] Crude lac resin contains up to 30% of **1**, which is



isolated by a simple extraction with base.[4] Oxidative cleavage of **1** with metaperiodate affords methyl azealdehydate (**2**) and 7-hydroxyheptanal (**3**).[5] A synthesis of the synthon **4**, a popular intermediate for prostaglandin syntheses,[6] has been achieved from cyclopentanone and the hydroxyaldehyde **3**.[5] Since azealdehydic acid is a byproduct of this synthesis, we examined the possibility that **2** might also be a synthon for prostaglandins. The present report demonstrates the feasibility of a complementary synthesis of **4** from **2** (see Scheme I).

Completion of the carbon skeleton of **4** is achieved by chemoselective reaction at −45 °C of the Grignard reagent **5** with the aldehydic carbonyl group in **2**. Chromic acid oxidation[7] of the hydroxyl in **6** to a carbonyl group and oxidative cleavage[8] of the olefin **7** affords γ-keto aldehyde **8**. Cyclodehydration of **8** gives methyl 7-(5-oxocyclopentenyl)heptanoate (**4**) in 35% overall yield from **2**.[9,10]

Scheme I



Experimental Section

Methyl Azealdehydate (2). A solution of potassium periodate (6.0 g) in 1 N H_2SO_4 (300 mL) at 20 °C was added rapidly to a vigorously stirred solution of trihydroxypalmitic acid (8.0 g) in a methanol–water solution (200 mL:200 mL) at 40 °C. After 10 min, the mixture was cooled to 15 °C in a methanol–ice bath and the solution was extracted immediately with ether (2 × 400 mL). The combined organic layers were extracted with saturated $NaHCO_3$ (2 × 100 mL), and the combined aqueous layers were acidified with concentrated HCl. The acidic aqueous solution was then extracted with ether (2 × 100 mL), and the combined ether layers were washed with brine (2 × 100 mL) and dried ($MgSO_4$). Removal of the solvent yielded 3.9 g (93%) of 95% pure product. The acid was then esterified with diazomethane (94%): bp 86–92 °C (0.2 mm);[11] NMR (CCl_4) δ 1.02–1.90 (10 H, m, $5CH_2$), 1.94–2.52 (4 H, m, $2CH_2$), 3.60 (3 H, s, CO_2CH_3), 8.70 (1 H, t, J = 2.4 Hz, CHO).

3-Butenyl-1-magnesium Bromide. Magnesium turnings (1.52 g), THF (5 mL; freshly distilled from benzophenone potassium ketyl), and 1-bromo-3-butene (1 mL of 5.1 mL total, 6.75 g, 0.05 mol) were placed in a flame-dried three-neck flask fitted with a reflux condenser, addition funnel, mechanical stirrer, and nitrogen inlet tube. When the reaction between the magnesium and bromide began, the remainder of the bromide in THF (45 mL) was added dropwise with stirring under nitrogen over a period of 1 h. After stirring at room temperature overnight, titration indicated an 83% yield.

Methyl 9-Hydroxy-12-tridecenoate (6). Methyl azealdehydate (70 g, 0.374 mol) and THF (500 mL; freshly distilled from benzophenone potassium ketyl) were added to a flame-dried three-neck flask fitted with a nitrogen inlet, addition funnel, low-temperature thermometer, and mechanical stirrer. The mixture was stirred under nitrogen and cooled to −45 °C, and the Grignard reagent from 3-butenyl bromide (200 mL of a 0.88 M solution) was added dropwise over a period of 1 h. The temperature of −45 °C was maintained throughout the addition. The mixture was stirred for 3 h at −40 °C, quenched by the dropwise addition of saturated NH_4Cl (100 mL), and allowed to warm to room temperature. Additional saturated NH_4Cl (200 mL) was added, and the mixture was extracted with ether (3 × 100 mL). The combined organic fractions were washed with saturated $NaHCO_3$ and brine and dried ($MgSO_4$). Distillation gave 42.0 g of recovered starting material **2** and 19.8 g (54%) of **6**: bp 115–120 °C (0.2 mm); ^1H NMR (CCl_4) δ 1.08–1.89 (12 H, broad m, $6CH_2$), 1.90–2.50 (6 H, m, $3CH_2$), 2.70 (1 H, broad s, OH), 3.61 (3 H, s, CO_2CH_3), 3.60–3.70 (1 H, m, CH), 4.73–5.21 (2 H, m, vinyl CH_2), 5.47–6.08 (1 H, m, vinyl CH).

Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.37; H, 10.81. Found: C, 69.32; H, 11.09.

Methyl 9-Oxo-12-tridecenoate (7). An aqueous chromic acid solution prepared from sodium dichromate dihydrate (5.0 g, 16.8 mmol) and 96% sulfuric acid (3.75 mL, 67 mmol diluted to 25 mL) was added dropwise to a stirred solution of **1** (9.5 g, 40.1 mmol) and ether (25 mL) in a 100-mL three-neck flask fitted with an addition funnel, reflux condenser, and magnetic stirring bar. Addition was performed over a 15-min period and the temperature maintained at 25 °C

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