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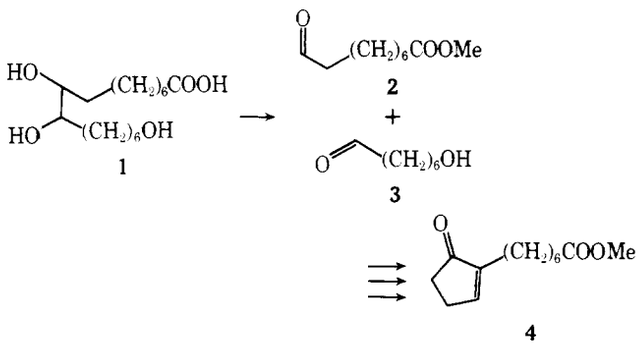
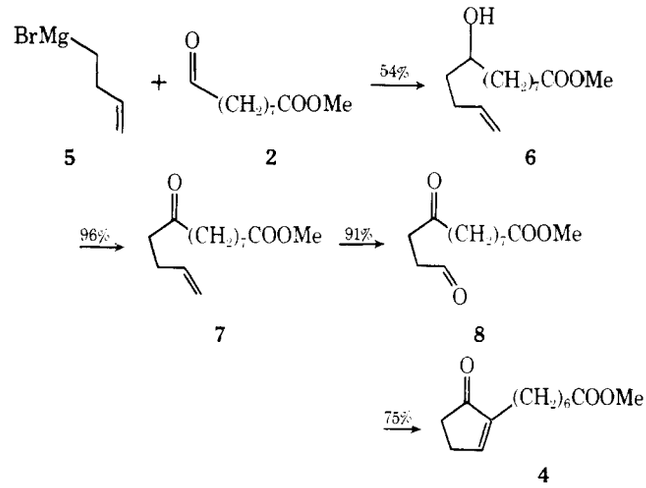
An attractive strategy for the construction of valuable prostanoids exploits readily available synthons derived from natural products.[1] Aleuritic acid (**1**) is a major component of shellac.[2,3] Crude lac resin contains up to 30% of **1**, which is



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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(cooling with an ice bath was required). After 2 h, the upper layer was separated and the aqueous phase was extracted with ether (2 × 50 mL). The combined organic extracts were washed with saturated sodium bicarbonate and brine and dried ($MgSO_4$). Removal of the solvent under reduced pressure yielded 9.0 g (96%) of **7**: NMR (CCl_4) δ 1.05–1.85 (12 H, broad m, $6CH_2$), 2.06–2.50 (6 H, m, $3CH_2$), 3.60 (3 H, s, CO_2CH_3), 4.72–5.18 (2 H, m, vinyl CH_2), 5.45–6.12 (1 H, m, vinyl CH).

Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06. Found: C, 70.24; H, 10.23.

Methyl 9-Oxo-12-dodecanaloate (8). A three-neck round-bottom flask fitted with a mechanical stirrer was charged with *tert*-butyl alcohol (60 mL), water (20 mL), **5** (4.32 g, 17.8 mmol), and osmium tetroxide (45.2 mg, 0.17 mmol in *tert*-butyl alcohol). The resulting solution was stirred for 5 min. A temperature of 24–26 °C was maintained with ice bath cooling during the addition of sodium metaperiodate (8.24 g, finely divided) in small portions over a period of 30 min. The tan-colored slurry was stirred at ambient temperature for an additional 4 h. At the end of this period the precipitate was white. The reaction mixture was extracted thoroughly with ether (3 × 100 mL), and the combined organic layers were washed with saturated sodium sulfite, saturated $NaHCO_3$, and brine and dried (Na_2SO_4). Removal of the solvent under reduced pressure yielded 3.9 g (91%) of product: NMR (CCl_4) δ 1.04–1.83 (10 H, broad m, $5CH_2$), 2.10–2.55 (4 H, m, $2CH_2$), 2.61 (4 H, s, $COCH_2CH_2CO$), 3.61 (3 H, s, CO_2CH_3), 9.60 (1 H, s, CHO).[10]

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Registry No.—**1**, 533-87-9; **2**, 1931-63-1; **4**, 34546-57-1; **6**, 67237-57-4; **7**, 67237-58-5; **8**, 50266-44-9; 1-bromo-3-butene, 5162-44-7.

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An Efficient Conversion of Ketones to α,β-Unsaturated Ketones

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The C-alkylation of a terminal carbon in conjugated enamino ketones may be achieved through reaction with alkyl halides in the presence of *n*-butyllithium,[1] hydroxymethylation of acylated enamines with formaldehyde and an alkyllithium,[2] or through use of enamino ketones as nucleophilic acylating agents.[3,4]

We have now found that the reaction of structurally related β-acylenamines with alkyllithium reagents follows an alternative course to yield α,β-unsaturated carbonyl compounds. The problems associated with the synthesis of such compounds have been documented[5,6] and some particularly efficient methods have been developed for their preparation.[7] The work reported herein affords a practical, efficient route to α,β-unsaturated ketones in 60–85% yield based on starting ketone.

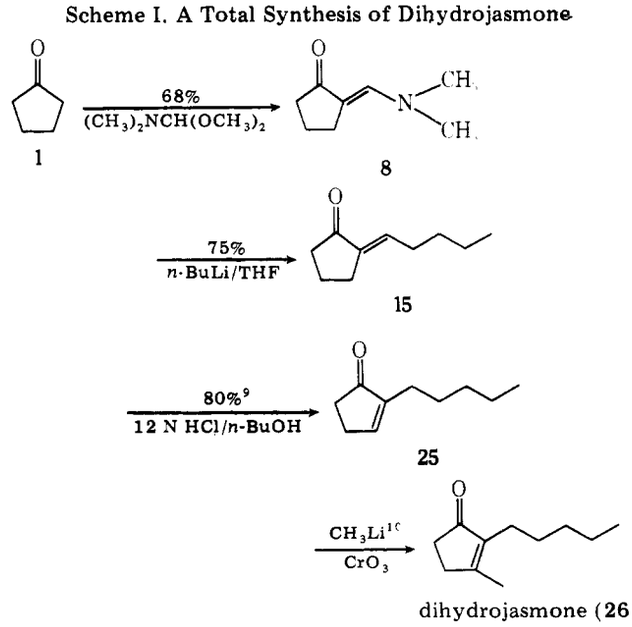
Condensation of ketones **1–7** with *N,N*-dimethylformamide dimethyl acetal at 110 °C for 12 h under nitrogen gave enamino ketones **8–14**, respectively.[8] When the enamino ketones were treated with 1.1 equiv of *n*-butyllithium in anhydrous tetrahydrofuran at −30 to 0 °C and then allowed to warm to room temperature, the corresponding α,β-unsaturated ketones **15–24** were obtained (Table I).

In order to demonstrate the versatility of this synthetic method, we have applied the sequence to prepare several natural products of which dihydrojasmone (**26**) and perillaketone (**30**), originally isolated from *Perilla frutescens* Brit.,[13] are representative examples.

The conversion of *N,N*-dimethylatropaldehyde (**31**)[12] to the unsaturated aldehyde (**32**) in 70% yield without any concomitant carbinol formation would serve to indicate that the course of these reactions is not sterically determined. Furthermore, the absence of any additional attack on the α,β-unsaturated carbonyl compounds by alkyllithium is believed due to the intervention of intermediates such as **33** which have no propensity for additional attack by nucleophiles.

The generality of the process is demonstrated by successful extension to methyllithium and *tert*-butyllithium reagents

Scheme I. A Total Synthesis of Dihydrojasmone



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