

9-Acetate $\bar{\nu}_{\max}$ 1720–1740 cm^{-1} (film); ^1H NMR δ 2.08, 2.13, 2.30, 3.57 and 3.83 (each 3 H, s), 3.01, 3.11 and 5.34 (each 1 H, ABX, $J_{AB} = 16$ Hz, $J_{AX} = 9$ Hz, $J_{BX} = 5$ Hz), 5.10 (2 H, s), 6.63 (2 H, br s); ^{13}C NMR δ 20.53 and 21.18 (CH_3COO and CH_3Ar), 26.90 ($\text{CH}_3\text{CO-C}$), 31.45 (CH_2Ar), 26.90 and 31.45 ($2 \times \text{CH}_2\text{O}$), 78.50 (CHOAc), 99.15 (OCH_2O), 112.41 (arom. C-4), 123.32 (arom. C-6), 129.69 and 133.85 (arom. C-1 and C-5), 142.55 (arom. C-2), 151.78 (arom. C-3), 170.36 (CH_3COO), 205.44 ($\text{CH}_3\text{CO-C}$); m/e 310 (16 %, M^+).

4-Hydroxy-3-(3-methoxy-2-methoxymethoxy-5-methylphenyl)-2-butanone 10 (0.16 g, 18 %); $\bar{\nu}_{\max}$ 3450, 1720 cm^{-1} (film); ^1H NMR δ 2.07, 2.27, 3.57 and 3.82 (each 3 H, s), 3.9 (3 H, m), 5.11 (2 H, s), 6.45 and 6.68 (each 1 H, br s).

10-Acetate $\bar{\nu}_{\max}$ 1720–1745 cm^{-1} (film); ^1H NMR δ 2.00, 2.10, 2.27, 3.60 and 3.86 (each 3 H, s), 4.45 (3 H, m), 5.12 (2 H, s), 6.52 and 6.73 (each 1 H, br s); ^{13}C NMR δ 20.53 and 20.99 (CH_3COO and CH_3Ar), 28.85 ($\text{CH}_3\text{CO-C}$), 50.03 (CHAr), 55.42 and 57.24 ($2 \times \text{CH}_2\text{O}$), 63.80 (CH_2OAc), 99.15 (OCH_2O), 112.66 (arom. C-4), 119.81 (arom. C-6), 128.65 and 134.43 (arom. C-1 and C-5), 142.09 (arom. C-2), 151.84 (arom. C-3), 183.41 (CH_3COO), 205.84 ($\text{CH}_3\text{CO-C}$); m/e 310 (13 %, M^+).

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C=C Ozonolysis with Concomitant Introduction of Ester α,β -Unsaturation. A Short Synthesis of (*E*)-10-Hydroxy-2-decenoic Acid (Royal Jelly Acid) and of (*E*)-2-Decenedioic Acid

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The selenoxide *syn* elimination is a highly efficient method for the stereoselective introduction of carbonyl α,β -unsaturation.¹ The oxidation of the intermediate α -phenylselenide may be carried out with ozone, among other reagents. It appeared probable that this reaction could be combined in a one-pot operation with the ozonolysis of another double bond present in the same molecule. At low temperatures, the selenoxide formed would probably be stable while the double bond is being attacked, and should eliminate only at or near room temperature, thus yielding the α,β -enoic system, which in turn should be stable towards the usual ozonide reduction or oxidation reagents.

We now report that the above speculations can indeed be realised to provide the generalized transformation 1 \rightarrow 2, involving overall a demologation with oxidative transposition of the double bond.

By way of illustration, the above sequence provides a very short synthesis of esters of (*E*)-10-hydroxy-2-decenoic acid (3) and (*E*)-2-decenedioic acid (4), compounds involved in honeybee biochemistry.² The former is the well-known royal jelly acid, a substance possessing antibiotic³ and antitumour⁴ properties and the object of numerous syntheses in the past.*

Thus, ethyl 10-undecenoate (5) was converted to the α -phenylselenide (6) which was directly treated, after change of solvent, with ozone at -78°C followed by sodium borohydride at room temperature, giving ethyl (*E*)-10-hydroxy-2-decenoate (3) in 46 % yield. Replacing sodium borohydride in the last step by peracetic acid gave the ethyl hydrogen (*E*)-2-decenedioate (4) in 26 % yield. An improved yield (58 % overall) of 4 is obtained by first treating the ozonide with triethyl phosphite followed by isolation of the aldehyde (7) (68 %) which is then oxidised to 4 (pyridinium dichromate in DMF⁵).

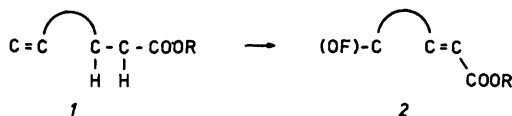
Experimental. Ethyl (*E*)-10-hydroxy-2-decenoate 3. Ethyl 10-undecenoate (K & K Chemicals) (1.5 g, 7 mmol) in dry tetrahydrofuran (THF) (35 ml) was added dropwise with stirring into 8 mmol of lithium diisopropylamide (from 1.13 ml of diisopropylamine and 3.4 ml of 2.14 M

* For recent syntheses of 3 and 4, and references to earlier work, see Refs. 5–7.

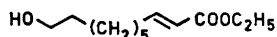
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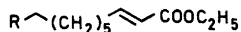
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(OF) = oxygen functionality

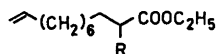


3



4 R = COOH

7 R = CHO



5 R = H

6 R = SeC₆H₅

BuLi—hexane in 35 ml of THF) under Ar at -78°C . After 10 min, 7.5 mmol of PhSeBr (from 1.17 g Ph₂Se₂ and 0.2 ml of Br₂ in 15 ml of THF) was added dropwise. The reaction mixture was allowed to warm to room temperature, the solvent removed and dry CH₂Cl₂ (50 ml) added. The mixture was again cooled to -78°C and ozone in air led in until all starting material was consumed (TLC). The solution was then allowed to warm to room temperature and the solvent replaced by H₂O—THF (1:2, 50 ml). Sodium borohydride (0.25 g) was added and the solution stirred at ambient temperature for 1 h. Ether (100 ml) was added and the solution washed with 1 N HCl, saturated NaHCO₃ and water. The product 3 was isolated using preparative TLC (Merck silica gel PF₂₅₅, elution with chloroform) in 46 % yield (0.64 g), and had spectral characteristics (MS, IR, NMR) as reported.⁵

Ethyl hydrogen (E)-2-decene-1,10-dioate 4.

A. Peracetic acid (40 %, 1.33 ml, 7 mmol) was added to the above ozonide solution in CH₂Cl₂ at -78°C , and the solution was then kept overnight at ambient temperature followed by washing with water. Extraction with NaHCO₃ solution and acidification gave 0.40 g (26 %) of oily 4, δ 2.2 (4 H, m), 5.8 (1 H, d, $J = 16$ Hz), 6.90 (1 H, d of t, $J = 16$ and 6.5 Hz), 9.9 (1 H, br s, exch. D₂O) + -COOC₂H₅ peaks at 1.2 and 4.1; m/e (of methyl ester) 242 (5 %).

B. *Via the aldehyde* 7. Trimethyl phosphite (1.3 g, 10.5 mmol) was added to the ozonide solution in CH₂Cl₂ at -78°C and the mixture stirred overnight at ambient temperature. The aldehyde was isolated using preparative TLC in 68 % yield (0.95 g), δ 9.8 (1 H, t, $J = 1$ Hz). Oxidation of the aldehyde with pyridinium dichromate⁸ gave 4 (0.87 g, 85 % from 7).

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