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SYNTHESIS OF 2-DECENEDIOIC ACID (ROYAL JELLY ACID) BY SEQUENTIAL CARBONYLATION OF BUTADIENE CATALYZED BY A PALLADIUM–PHOSPHINE COMPLEX AND DICOBALT OCTACARBONYL

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Summary

Carbonylation of butadiene in *t*-butyl alcohol catalyzed by a palladium complex gave *t*-butyl-3,8-nonadienoate (I). Further carbonylation of I in methanol with $\text{Co}_2(\text{CO})_8$ afforded *t*-butylmethyl-3-decenedioate (II) as the main product. Hydrolysis and base-catalyzed isomerization of II produced *E*-2-decenedioic acid.

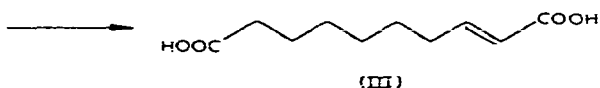
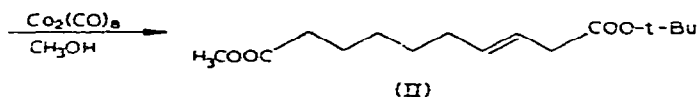
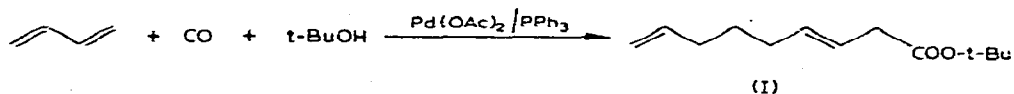
Introduction

Royal jelly is the sole nutrient of queen bee larvae and investigation of the lipids of royal jelly has shown that the free fatty acid fraction is a complex mixture of C_{10} acids, called royal jelly acids, one of which is *E*-2-decenedioic acid (III) [1,2]. The acid also was isolated from mold *Penicillium Notatum* together with penicillin [3,4]. Brown and Freure synthesized 2-decenedioic acid in low yield by the oxidation of 10-hydroxy-2-decenoic acid, which is a main component of the royal jelly acids [1]. We now wish to report the facile synthesis of this acid by sequential carbonylation of butadiene catalyzed by a palladium–phosphine complex and by $\text{Co}_2(\text{CO})_8$.

Results

The acid was synthesized by palladium-catalyzed carbonylation of butadiene to give 3,8-nonadienoate (I), followed by selective carbonylation of the terminal double bond with $\text{Co}_2(\text{CO})_8$ as a catalyst to give 3-decenedioate (II). The final step is base-catalyzed isomerization of the double bond at position 3 to the conjugated position.

The carbonylation of butadiene using $\text{Pd}(\text{OAc})_2$ and PPh_3 as catalyst was



carried out as reported previously by us [5] and Billups et al. [6] in *t*-butyl alcohol to give *t*-butyl-3,8-nonadienoate (I) in 90% yield. The next step was the carbonylation of the terminal double bond of I to give the linear diester rather than the branched diester with high selectivity. For selective linear carbonylation of terminal olefins, a platinum catalyst has been reported to be effective [7]. Also, $\text{Co}_2(\text{CO})_8$ combined with pyridine is known to produce a high ratio of linear/branched esters under mild conditions [8]. In this study, the carbonylation of I was carried out with $\text{Co}_2(\text{CO})_8$.

The monoester I was carbonylated in a mixture of methanol and benzene using $\text{Co}_2(\text{CO})_8$ as catalyst in the presence of pyridine at 90°C under low carbon monoxide pressure. Gas-chromatographic analysis of the reaction mixture showed that the conversion of monoester I to diester II was 62%. The ratio of the linear and branched diesters was found to be 4 : 1. The desired linear diester II was isolated by fractional distillation.

Mild hydrolysis of the diester II, followed by recrystallization of the crude acid, produced *E*-3-decenedioic acid. The base-catalyzed isomerization of 3-decenedioic acid to 2-decenedioic acid (III) was carried out under more severe conditions until equilibrium was reached. After the isomerization, the basic solution was acidified and a crude mixture of 2- and 3-decenedioic acids was obtained. A small amount of the mixed acids was methylated with diazomethane. Gas-chromatographic analysis of the mixed esters showed that the ratio of dimethyl 2- and 3-decenedioate was 2 : 1. Separation of 2-decenedioic acid from 3-decenedioic acid was achieved by recrystallization. The more easily crystallizable, high melting 2-decenedioic acid was obtained preferentially. The mother liquor of the recrystallization was evaporated and the residue was subjected again to the base catalyzed isomerization and recrystallization to give pure 2-decenedioic acid in a combined yield of 80%. Thus the method reported in this paper offers a simple synthetic method of the royal jelly acid.

Experimental

t-Butyl-3,8-nonadienoate

As reported previously [5], butadiene (20 g) was carbonylated in *t*-butyl

alcohol (30 ml) using $\text{Pd}(\text{OAc})_2$ (0.3 g) and PPh_3 (0.7 g) under carbon monoxide pressure (50 atm) at 110°C for 15 h to give *t*-butyl-3,8-nonadienoate (40 g, 90%), b.p. $90\text{--}94^\circ\text{C}/1\text{ mmHg}$.

Carbonylation of t-butyl-3,8-nonadienoate

A mixture of the monoester I (6.3 g, 30 mmol), benzene (40 ml), methanol (1.5 g), $\text{Co}_2(\text{CO})_8$ (1.03 g, 3 mmol), and pyridine (0.94 g, 12 mmol) was placed in a 100 ml stainless steel autoclave. Carbon monoxide was introduced to 16 atm. The autoclave was placed in an oil bath kept at 90°C and stirred by a magnetic stirrer for 42 h. Then the solvent was removed and the residue was fractionally distilled. The desired *t*-butylmethyl-3-decenedioate, was obtained at $107^\circ\text{C}/1\text{ mmHg}$ (2.88 g, 57% based on the consumed monoester; $^1\text{H NMR}$ (CCl_4), δ 5.48 (m, 2H), 3.60 (s, 3H), 2.85(d, 2H), 2.15(m, 4H), 1.40(s, 15H) ppm.

3-Decenedioic acid

The diester II (0.5 g) was hydrolyzed with 10% ethanolic NaOH (3 ml) at room temperature for 60 h. The basic solution was acidified and the crude acid (0.3 g, 80%) was recrystallized from benzene to produce *E*-3-decenedioic acid as colorless crystals. m.p. $105\text{--}105.5^\circ\text{C}$, Anal. Found: C, 59.63; H, 8.49. $\text{C}_{10}\text{H}_{16}\text{O}_4$ calcd.: C, 59.98; H, 8.06%. $^1\text{H NMR}$ (CDCl_3), δ 9.4 (s, 2H), 5.6 (m, 2H), 3.1(d, 2H) ppm. The purity of the acid was confirmed by gas chromatography after converting it to the dimethyl ester with diazomethane.

2-Decenedioic acid

3-Decenedioic acid (1.14 g) was heated in a sealed tube with 10 ml of 10 *N* NaOH at 120°C for 20 h. The solution was acidified and a crude mixture of 2- and 3-decenedioic acids was obtained. Recrystallization of the mixed acids from hexane/ethyl acetate produced 2-decenedioic acid preferentially. The mother liquor of the recrystallization was evaporated and the residue was subjected to the isomerization and recrystallization again. Pure 2-decenedioic acid was collected in a total yield of 79.8% (0.91 g). M.p. $168\text{--}170^\circ\text{C}$, reported, $169\text{--}170^\circ\text{C}$ [2,4], $172\text{--}173^\circ\text{C}$ [1,3]. Anal. Found: C, 60.20; H, 8.08. $\text{C}_{10}\text{H}_{16}\text{O}_4$ calcd.: C, 59.98; H, 8.06%. $^1\text{H NMR}$ (CCl_4) spectrum of the dimethyl ester of III: δ 6.80 (m, 1H), 5.70 (d, 1H), 3.65 (s, 3H), 3.60 (s, 3H), 2.20 (m, 4H), 1.38 (broad 8H) ppm.

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