BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 51 (6), 1915—1916 (1978)

A Simple Synthetic Method for 2,15-Hexadecanedione from a Butadiene Telomer

Jiro TSUJI,* Mitsumasa KAITO, Toshiro YAMADA, and Tadakatsu MANDAI
Tokyo Institute of Technology, Meguro, Tokyo 152

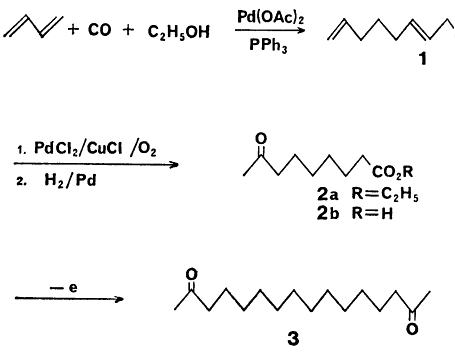
(Received January 20, 1978)

Synopsis. The terminal double bond of 3,8-nonadienoate was oxidized to methyl ketone with a catalyst system of $PdCl_2/CuCl/O_2$ and the internal double bond was reduced to give 8-oxononanoate, which was hydrolyzed to 8-oxononanoic acid. The Kolbe electrolysis of the acid produced 2,15-hexadecanedione in a high yield.

Palladium compounds are useful reagents for organic synthesis. Particularly there are two useful synthetic reactions catalyzed by palladium compounds. They are oxidation of olefins catalyzed by $Pd(II)/Cu(II)/O_2$ system to carbonyl compounds,[1-3] and telomerization of butadiene with nucleophiles catalyzed by palladium-phosphine complexes.[4]

We now wish to report the application of these two palladium catalyzed reactions to the synthesis of 2,15-hexadecanedione (**3**). The conversion of this diketone to muscone by aldol condensation had been reported by Stoll.[5] One drawback of the Stoll method is a low yield of the intramolecular aldol condensation, which competes with the intermolecular reaction. In order to make this method more useful and make up for the low yield of the aldol condensation, it is essential to synthesize the diketone **3** as the precursor easily in high yield. We have already reported the synthesis of the diketone **3** by coupling a C_8 chain, which is easily available by the palladium catalyzed telomerization of butadiene with acetic acid.[6,7]

The present method shown below utilizes a C_9 acid **2b** which was coupled by the Kolbe reaction. The method is simpler and gave a higher overall yield.



We have reported the dimerization-carbonylation of butadiene catalyzed by a system of palladium acetate and triphenylphosphine to give 3,8-nonadienoate (**1**) in a high yield.[8,9] In the present studies, this C_9 ester was converted into the C_{16} diketone as shown in the above scheme. The Kolbe coupling of 8-oxononanoic acid (**2b**) has been claimed by Tsuzuki and Motoki in a patent.[10] However, in their method, the acid **2b** was synthesized by the cross Kolbe reaction of adipic acid and levulinic acid, which gave inevitably a mixture of coupled products.[10,11] In the present method the easily available C_9 ester **1** is the starting material.

At first the terminal double bond of **1** was oxidized to a methyl ketone using $PdCl_2/CuCl/O_2$ as a catalyst system at room temperature in *N,N*-dimethylformamide.[12] Ethyl 8-oxo-3-nonenoate was isolated by distillation in 86.7% yield. The internal double bond which remained intact during the oxidation was hydrogenated by using palladium on carbon as a catalyst to give ethyl 8-oxononanoate in 98% yield. The ester was then hydrolyzed with methanolic KOH to give 8-oxononanoic acid as crystals in 92% yield. The final step of the synthesis is the Kolbe electrolysis. The sodium salt of the keto acid **2b** in methanol was subjected to Kolbe electrolysis using Pt electrode at 0° C. After the reaction, a neutral fraction was isolated by the usual work-up as a solid material which was recrystallized from methanol to afford the diketone **3** as colorless crystals in 63% yield. The diketone was identified by its mp and NMR spectral data.

Experimental

Melting points were measured on a Shibata (No. 297) melting point apparatus. The IR spectra were taken on a JASCO (IRA-2) spectrophotometer. The NMR spectra were taken on a HITACHI (R-24A) spectrometer (60 MHz) with tetramethylsilane as an internal reference.

Materials. Ethyl 3,8-nonadienoate (**1**) was prepared by the reaction of butadiene with carbon monoxide and ethanol using palladium acetate and triphenylphosphine as a catalyst under pressure of carbon monoxide,[8] bp 60—63 °C/4 Torr: IR (neat) 2980, 2920, 1740, 1640, 1160, 970, 910 cm^{-1}; NMR (CCl_4) δ 5.3—6.1 (m, 3H), 4.7—5.1 (m, 2H), 4.0 (q, J=7 Hz, 2H), 2.8—3.1 (m, 2H), 1.8—2.3 (m, 4H), 1.55 (t, J=6 Hz, 2H), 1.2 (t, J=7 Hz, 3H).

Oxidation of Ethyl 3,8-Nonadienoate. A mixture of $PdCl_2$ (877 mg, 4.95 mmol) and CuCl (4.90 g, 49.6 mmol) in aqueous *N,N*-dimethylformamide (25 ml, H_2O, 3 ml) was shaken in a 100 ml glass vessel under oxygen atmosphere for 1 h. Then the ester **1** (8.96 g, 49.2 mmol) was added and the mixture was shaken under oxygen atmosphere at room temperature for 5 h. The solution was poured into dilute hydrochloric acid and the resulting mixture was extracted with dichloromethane. Ethyl 8-oxo-3-nonenoate was isolated by distillation (8.44 g, 86.7%): bp 86—87 °C/5 Torr; NMR (CCl_4) δ 5.3—5.5 (m, 2H), 4.0 (q, J=7 Hz, 2H), 2.8—3.0 (m, 2H), 2.35 (t, J=6.5 Hz), 2.0 (s 3H), 1.4—2.1 (m, 4H), 1.2 (t, J=7 Hz, 3H); IR (neat) 2980, 2940, 1735, 1715, 1370, 1250, 1165, 1030, 970 cm^{-1}.

Hydrogenation of Ethyl 8-Oxo-3-nonenoate. Ethyl 8-oxo-3-nonenoate (2.88 g, 14.5 mmol) was dissolved in ethanol (20 ml) in a 50 ml flask and palladium on carbon (5%, 80 mg) was added. The resulting mixture was shaken under atmospheric pressure of hydrogen at room temperature for

3 h. The mixture was filtered and the solvent was removed to give crude ethyl 8-oxonoanoate (**2a**) (2.85 g, 98%): NMR (CCl_4) δ 4.0 (q, J=7 Hz, 2H), 2.2 (t, J=8 Hz, 4H), 2.05 (s, 3H), 1.0—1.7 (broad, 11H).

Hydrolysis of Ethyl 8-Oxononanoate. Ethyl 8-oxononanoate (17.7 g, 88.5 mmol) was dissolved in methanol (30 ml) in a 200 ml flask and an aqueous KOH solution (5.0 g, 89.3 mmol in 100 ml of H_2O) was added and the solution was stirred for 3 h. After the usual work-up, crude 8-oxononanoic acid (**2b**) (14.1 g, 82.0 mmol, 92%) was obtained. The acid **2b** was purified by recrystallization from hexane and benzene to give colorless needles, mp 42.5—44 °C (reported 40°C[13]): NMR (CCl_4) δ 11.3 (s, $-CO_2H$, 1H), 2.35 (t. J= 6 Hz, 2H), 2.30 (t, J=6 Hz, 2H), 2.1 (s, 3H), 1.0—1.9 (broad, 8H).

Kolbe Electrolysis. 8-Oxononanoic acid (6.28 g, 36.6 mmol) in sodium methoxide solution (50 mg of Na in 70 ml of MeOH) was placed in a 100 ml glass vessel equipped with a Pt electrode and a magnetic bar. The electrolysis was carried out with stirring at 0 °C under nitrogen atmosphere (65 volt, 0.2—0.6 ampere) for 2 h. After the reaction, precipitated white solid was filtered and the filtrate was concentrated. The residue was poured into an aqueous $NaHCO_3$ solution and the solution was extracted with dichloromethane. The dichloromethane solution was washed with brine and dried over $MgSO_4$. After removal of the solvent, white solid was obtained which was recrystallized from methanol to afford 2,15-hexadecanedione (**3**) as colorless crystals, 2.93 g, 63%, mp 83.5—85.0 °C, (reported 83—84 °C)[11]: NMR (CCl_4) δ 2.1—2.4 (t, J=7 Hz, 4H), 1.95 (s, 6H), 1.0—1.7 (broad, 20H); IR (KBr disk) 2900, 2830, 1710, 1460, 1160, 800, 720, 600 cm^{-1}.

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