

4,7-Dioxooctanoic Acid from the Acid Catalysed Reaction of (*E*)-4-(2-furyl)but-3-enone. Electrochemical Hydrogenation of some Furan Derivatives

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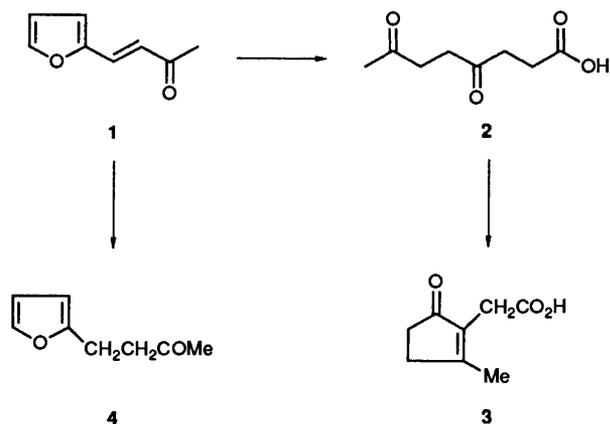
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A two phase acidic reaction medium has been developed for the conversion of (*E*)-4-(2-furyl)but-3-enone into 4,7-dioxooctanoic acid in consistent yields of 50% with concomitant formation of 15% polymer. The corresponding ring opening of 1-(2-furyl)-5-methylhex-1-en-3-one proceeds in homogeneous acid solution in very high yield without polymer formation. The two furylalkenones can be reduced electrochemically to the corresponding furylalkylketones in good yields at a lead cathode in the presence of sodium hydrogen carbonate.

The one step acid catalysed ring opening of (*E*)-4-(2-furyl)but-3-enone **1** to yield 4,7-dioxooctanoic acid **2** is potentially very useful because the starting material is readily available and the product can be cyclised in good yield to the cyclopentenone **3**.¹ This cyclopentenone is an intermediate in one synthesis of jasmone.²

Hunsdiecker,¹ who first reported the ring opening of **1**, indicated poor yields of product. Later workers³ claimed yields of 50% but Birch,² following the reports, could only obtain 35–43% yields after a long and tedious reaction procedure. In our hands these methods applied to (*E*)-4-(2-furyl)but-3-enone yielded mostly polymer and no more than 3–5% of **2**.



Results

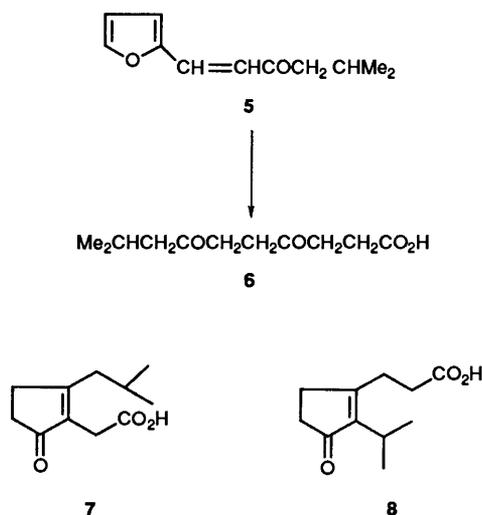
Seeking another route to 4,7-dioxooctanoic acid, we examined the oxidative ring opening of 4-(2-furyl)butanone **4**. This ketone is conveniently prepared by the electrochemical reduction of (*E*)-4-(2-furyl)but-3-enone with sodium hydrogen carbonate as electrolyte in a modification of the procedure of Shima.⁴ We have also applied the electrochemical hydrogenation step to the enone **5**. Reduction of the furan ring or the carbonyl group was not observed in these reactions.

A mixture of chromium trioxide and pyridine in dichloromethane has been used for the oxidative ring opening of furans.² However, oxidation of 4-(2-furyl)butanone led to destruction of the furan ring and 4-oxopentanoic acid was the only product isolated. This approach was therefore abandoned.

A rational procedure for avoiding the formation of polymer during the acid catalysed conversion of **1** into **2** came from a knowledge of the properties of furfuryl alcohol. Thus,

Pummerer⁵ has shown that furfuryl alcohol in low concentrations is converted by acid into laevulinic acid while, at high concentrations of furfuryl alcohol, polymerisation predominates. His work suggests that if a convenient process for regulating the concentration of (*E*)-4-(2-furyl)but-3-enone in aqueous acid can be developed then the yield of **2** from the reaction will be substantially increased.

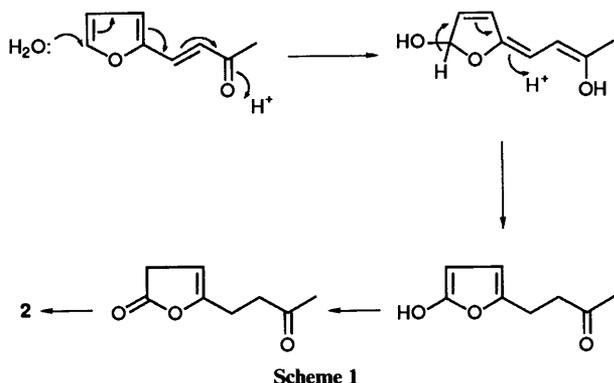
Our convenient procedure for the acid catalysed ring opening process uses a two phase system of cyclohexane and aqueous hydrochloric acid as the reaction medium. The starting material dissolves in the cyclohexane layer and is then slowly fed into the aqueous layer where the hydrolysis takes place. At the end of the reaction the insoluble polymeric products were collected while the soluble material was separated into a base soluble fraction containing **2** and a neutral residue of unchanged **1**. Optimisation of the amounts of co-solvents, acetic acid and methanol, gave a procedure for converting **1** into **2** in consistent yields of ca. 50%. The yield is sensitive to the contact area between the cyclohexane and water phases. Good contact is obtained by using a wide-bodied flask and by vigorous stirring. The function of the co-solvent appears to be to speed up the desired reaction.



The analogous conversion of **5** into **6** was slow under the above conditions and much starting material remained. However, this conversion is conveniently effected in homogeneous solution. We used methanol as a co-solvent and isolated a high total yield of the acid **6** and its methyl ester. No polymer was

formed. Base catalysed cyclisation of either the acid **6** or its methyl ester afforded the same mixture of two cyclopentenones **7** and **8**.

The acid catalysed conversion of **1** into **2** can be rationalised by protonation of **1** at the carbonyl centre followed by the reaction sequence shown in Scheme 1.



Experimental

¹H NMR spectra were obtained in CDCl₃ on a General Electric 300 MHz instrument. Coupling contents are in Hz.

(*E*)-4-(2-Furyl)but-3-enone **1**.—This compound, prepared according to the literature,⁶ was obtained as yellow crystals, m.p. 35–37 °C (lit.,⁶ m.p. 35–37 °C), δ_{H} 2.40 (3 H, s, CH₃), 6.50 (1 H, m, furan), 6.63 (1 H, d, *J* 7, alkene), 6.68 (1 H, d, *J* 3, furan), 7.29 (1 H, d, *J* 17, alkene) and 7.52 (1 H, s, furan).

1-(2-Furyl)-5-methylhex-1-en-3-one **5**.—Freshly distilled 2-furaldehyde (60 g, 0.625 mol), 4-methylpentan-2-one (120 g, 1.2 mol) and water were mixed. A solution of aqueous sodium hydroxide (12.5 ml, 33%) was added with stirring and stirring continued for 3 h at 50 °C. Two layers formed after acidification with dilute sulphuric acid and the upper organic layer was separated and distilled under reduced pressure. The fraction (86 g, 77%) which distilled at 78–80 °C/0.001 mmHg (lit.,³ b.p. 116–117 °C/5 mmHg) was collected and identified as 1-(2-furyl)-5-methylhex-1-en-3-one; *m/z* 178 (M⁺), δ_{H} 0.98 (6 H, d, *J* 6, 2 × CH₃), 2.18 (1 H, 9 lines, *J* 6, CH), 2.49 (2 H, d, *J* 6, CH₂), 6.49 (1 H, d, *J* 3, furan), 6.65 (1 H, d, *J* 17, alkene), 6.67 (1 H, m, furan), 7.35 (1 H, d, *J* 17, alkene) and 7.50 (1 H, s, furan).

Electrochemical Hydrogenation.—The electrochemical cell used was a cylindrical glass vessel, diameter 7 cm, and of 350 ml capacity fitted with a rubber stopper. Suitable holes were drilled in the stopper so as to hold a porous cup along the cylinder axis, an outlet for gases and a lead to the cylindrical lead cathode placed between the porous pot and the walls of the glass vessel. Only one surface of the cylinder was considered in calculations of current density. A lead cylinder was introduced into the porous pot to serve as anode. The catholyte was agitated with a magnetic stirrer throughout the experiments. Experiments were conducted at constant current.

4-(2-Furyl)butanone **4**. A mixture of ethanol (50 ml) and water (100 ml) was introduced into the cathode chamber of the electrochemical cell. Solid sodium hydrogen carbonate was added to give a saturated solution. The porous pot was filled with a 10% solution of sodium hydroxide in ethanol–water (1:1) and an external potential was applied between the two electrodes to obtain the current density of 0.06 A cm². (*E*)-4-(2-Furyl)but-3-enone (14 g), dissolved in ethanol (50 ml) was then slowly introduced to the cathode chamber over 1 h after which the reduction was continued for a further 1 h. Solid sodium

hydrogen carbonate had to be introduced to the cathode solution from time to time to maintain saturation.

At the end of the reaction period the catholyte was extracted with ether. The diethyl extract was dried (Na₂SO₄) and evaporated under reduced pressure to leave 4-(2-furyl)butanone as a brown oil. In one trial the yield was determined as 90% by addition of a weighed aliquot of 1,4-dimethoxybenzene, and then integration of the ¹H NMR spectrum of the mixture. Distillation afforded 4-(2-furyl)butanone (20%) as a colourless liquid, b.p. 35–45 °C/0.01 mmHg (lit.,⁷ b.p. 100–104 °C/25 mmHg) (Found: C, 70.0; H, 7.4. Calc. for C₈H₁₀O₂: C, 69.5; H, 7.3%), which rapidly discoloured even at 0 °C. A black residue remained in the distillation flask. The product was more conveniently purified by chromatography over alumina and elution with ether. Overall yields of 57% were obtained by chromatography; δ_{H} 2.15 (3 H, s, CH₃), 2.78 (2 H, t, *J* 7, CH₂), 2.92 (2 H, t, *J* 7, CH₂), 6.00 (1 H, d, *J* 3, furan), 6.28 (1 H, m, furan) and 7.30 (1 H, s, furan).

1-(2-Furyl)-5-methylhexan-3-one.—1-(2-Furyl)-5-methylhex-1-en-3-one (14 g) was reduced at a lead cathode as described for the previous example and using a current density of 0.06 A cm⁻². The product was isolated in 59% yield by chromatography. Alternatively, distillation of the reaction mixture afforded 1-(2-furyl)-5-methylhexan-3-one as a pale yellow oil (37%), b.p. 87–89 °C/0.8 mmHg (lit.,⁸ b.p. 111–112 °C/9 mmHg) (Found: C, 72.7; H, 9.1. Calc. for C₁₁H₁₆O₂: C, 73.3; H, 8.9%); δ_{H} 0.92 (6 H, d, *J* 6, 2 × CH₃), 2.13 (1 H, 9 lines, *J* 6, CH), 2.29 (2 H, d, *J* 6, CH₂), 2.73 (2 H, t, *J* 6, CH₂), 2.92 (2 H, t, *J* 6, CH₂), 6.00 (1 H, d, *J* 3, furan), 6.27 (1 H, m, furan) and 7.29 (1 H, s, furan).

4,7-Dioxooctanoic Acid **2**.—A series of trial experiments, summarised in Table 1, were conducted. For each experiment (*E*)-4-(2-furyl)but-3-enone (3.0 g) was dissolved in cyclohexane. Acetic acid, hydrochloric acid, methanol and water were mixed and added to the previous solution in a 250 ml flask. The whole was heated and stirred under reflux on an oil bath for 24 h.

After reaction the solvents and acids were removed under reduced pressure to leave a black product. This was treated with saturated aqueous sodium hydrogen carbonate until there was no further evolution of carbon dioxide. Extraction of the mixture with diethyl ether afforded unchanged (*E*)-4-(2-furyl)but-3-enone, confirmed by the ¹H NMR spectrum. The aqueous layer left after extraction was acidified with 20% sulphuric acid and extracted with ethyl acetate. After drying (Na₂SO₄), the extract was filtered and evaporated under reduced pressure to leave a pale cream solid. Crystallisation from light petroleum (b.p. 60–80 °C)–ethyl acetate yielded 4,7-dioxooctanoic acid, m.p. 73–75 °C (lit.,¹ m.p. 75 °C); δ_{H} 2.20 (3 H, s, CH₃), 2.55 (2 H, t, *J* 7, CH₂), 2.75 (4 H, s, 2 × CH₂) and 2.78 (2 H, d, *J* 7, CH₂). The black material, insoluble in both diethyl ether and aqueous sodium hydrogen carbonate, was taken as polymer.

Large scale repetitions using the conditions of trial No. 5 indicated in Table 1 gave consistent yields of 4,7-dioxooctanoic acid (50%).

9-Methyl-4,7-dioxodecanoic Acid **6**.—Reaction of 1-(2-furyl)-5-methylhex-1-en-3-one as described for the above example gave low yields of the acidic product, a large recovery of starting material and no polymer. The following procedure proved satisfactory. A solution of 1-(2-furyl)-5-methylhex-1-en-3-one (15 g), acetic acid (125 ml), concentrated hydrochloric acid (75 ml), methanol (100 ml) and water (75 ml) was heated under reflux on an oil-bath for 24 h. Acids and solvents were then removed under reduced pressure. The residue was warmed with aqueous sodium hydrogen carbonate until alkaline to litmus and then extracted with diethyl ether. The layers were separated. The aqueous layer was acidified with sulphuric acid

Table 1 Trial runs for the conversion of (*E*)-4-(2-furyl)but-3-enone into 4,7-dioxooctanoic acid

No.	Cyclohexane (ml)	Water (ml)	HOAc (ml)	10 M HCl (ml)	MeOH (ml)	4,7-dioxoacid (%)	Recovered enone (%)	Polymer (%)
1	50	35	20	7.5	—	27	7	17
2	50	35	10	15	—	26	3	22
3	50	35	20	15	—	34	9	18
4	50	35	30	5	—	25	7	13
5	50	20	20	15	15	50	5	15

and the product extracted with ethyl acetate. Evaporation of the ethyl acetate, after drying (Na_2SO_4), afforded 9-methyl-4,7-dioxodecanoic acid as colourless plates (50%) which crystallised from ethyl acetate–light petroleum (b.p. 60–80 °C) as plates, m.p. 74–75 °C (lit.,³ m.p. 80 °C); m/z 214 (M^+) (Found: C, 61.3; H, 8.5. Calc. for $\text{C}_{11}\text{H}_{18}\text{O}_4$: C, 61.6; H, 8.4%); δ_{H} 0.94 (6 H, d, *J* 6, 2 × CH_3), 2.14 (1 H, 9 lines, CH), 2.33 (2 H, d, *J* 6, CH_2), 2.65 (2 H, t, *J* 6, CH_2), 2.71 (4 H, s, 2 × CH_2) and 2.81 (2 H, d, *J* 6, CH_2).

Evaporation of the diethyl ether layer insoluble in aqueous sodium hydrogen carbonate afforded methyl 9-methyl-4,7-dioxodecanoate (41%), identified by the following criteria: m/z 228 (M^+); δ_{H} as for the acid above with the addition of 3.68 (3 H, s, $\text{CH}_3\text{O}_2\text{C}$).

In separate experiments the methyl ester and the decanoic acid above were refluxed with 4% aqueous sodium hydroxide for 2 h. Acidification and diethyl ether extraction afforded an oil. Both preparations showed the same spectral properties. The oil was identified as a mixture of cyclopentenones **7** and **8** in a ratio 77:23 from the ^1H NMR spectrum. Compound **7**: δ_{H} 0.93 (6 H, d, *J* 7, 2 × CH_3), 1.98 (1 H, 9 lines, *J* 7, CHMe_2), 2.35 (2 H, d, *J* 7, CH_2CHMe_2) and 3.30 (2 H, s, $\text{CH}_2\text{CO}_2\text{H}$). Compound **8**: δ_{H} 1.68 (6 H, d, *J* 7, 2 × CH_3) and 2.8 (4 H, m, $\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$). Multiplets due to both components at δ 2.48 and 2.61.

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