SHORT PAPER

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The structure of a by-product obtained during the chloromethylation of methyl 2-furoate[†]

Patrick A. Finan,* Caroline M. Lardner and Paul T. O'Sullivan

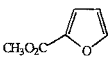
Chemistry Department, National University of Ireland, Galway, Ireland

The structure of a crystalline by-product obtained during the chloromethylation of methyl 2-furoate 1 has been established as 1,1-bis(2′-methoxyfuroyl-5′-methylenoexy) methane 5.

Treatment[1] of methyl-2-furoate **1** with paraformaldehyde, anhydrous zinc`chloride, and dry hydrogen chloride in chloroform at 35°C gave methyl 5-chloromethyl-2-furoate **2** as a distillable oil which subsequently crystallised (65% yield). The residue after the distillation gave a crystalline compound (10% yield) mp 76–78°C, to which we assign structure **5**.

A British patent[2] covering the preparation of esters of 5-chloroalkyl-2-furoic acid, *e.g.* **2**, has described that treatment of methyl-2-furoate **1** with formaldehyde, hydrogen chloride and zinc chloride in dichloromethane at 20 °C gave compound **2** (60% yield) as well as a higher boiling product (20–25% yield) formulated as **3**. When the chloromethylation reaction was carried out at 70°C in the absence of solvent, or in the presence of aluminium chloride and tetrachloromethane, in addition to **2**, a distillable product formulated as **4** was obtained. No supporting evidence was recorded for structures **3** and **4**.

The IR spectrum of compound **5** showed absorption for the ester carbonyl group (1731 m^{-1}) and for the furan ring (1602, 1543 cm^{-1}). The ^{1}H NMR spectrum had five types of proton signal in the ratio 3 : 2 : 1 : 1 : 1, whereas each of structures **3** and **4** had four types of proton. As well as doublet signals for 3′-H and 4′-H of the furan ring, and a singlet for the Me protons of the ester group, the spectrum showed signals for two distinct types of –CH$_2$O– group, *i.e.* $C - CH_2 - O - CH_2 - C$ and for –OCH$_2$O–. The ^{13}C NMR spectrum (aided by ^{13}C DEPT) fully supported structure **5**. The mass spectrum showed a molecular ion peak at *m/z* 324, corresponding to $C_{15}H_{16}O_8$. On the basis of the above evidence, the by-product was formulated as 1,1-bis (2′-methoxyfuroyl-5′-methyleneoxy) methane **5**.



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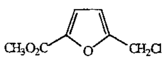

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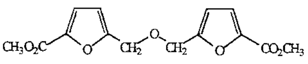

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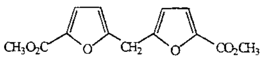

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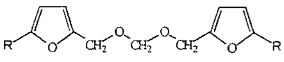
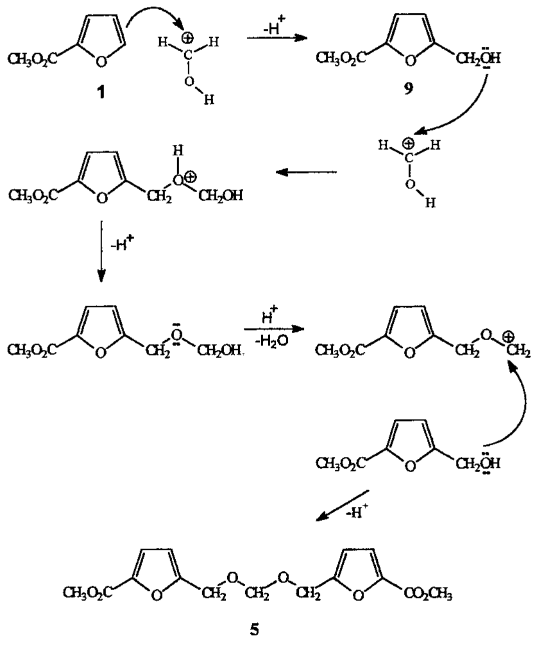


5 R = CO2CH3
6 R = CO2H
7 R = H
8 R = CHO

Saponification of the diester **5** with sodium hydroxide in aqueous ethanol gave a crystalline dicarboxylic acid, for which microanalytical data, IR, ^{1}H and ^{13}C NMR spectra agreed with structure **6**. The mass spectrum of **6** did not show a molecular ion peak; the highest *m/z* value was 207, which corresponded to the loss of two CO$_2$H groups from the parent molecule, with transfer of a hydrogen atom to the charged fragment. The base peak of the spectrum had *m/z* 81, corresponding to the furfuryl ion $(C_5H_5O)^+$. On heating with copper bronze in quinoline, acid **6** underwent decarboxylation[3] to give syrupy 1,1-bis (2′-furfuryloxy) methane **7**, whose structure was confirmed by ^{1}H and ^{13}C NMR spectra. Compound **7**, which represents the molecular core of by-product **5** was synthesised (70% yield) by reaction of furfuryl alcohol with dibromomethane in N,N-dimethylformamide in the presence of sodium hydride at room temperature. Using the Vilsmeier-Haak reaction,[4] compound **7** with phosphorous oxychloride and N,N-dimethylformamide, followed by a hydrolytic working up, gave the bis-formyl compound **8**. The latter was characterised on the basis of microanalytical data, ^{1}H and ^{13}C NMR spectra, and the preparation of crystalline 2,4-dinitrophenylhydrazone and semicarbazone derivatives. Oxidation of **8** with oxygen and a cuprous oxide – silver oxide catalyst[5] in alkaline medium gave the dicarboxylic acid **6**.

The production of the diester **5** having three CH$_2$ groups can be explained[6] as outlined in Scheme 1, with the protonated methanal species $^+CH_2OH$ playing a key role. Overall, the mechanism suggested resembles that which would be written for the acid-catalysed conversion of methanal into its acetal,



Scheme 1

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* To receive any correspondence.

[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

with the alcohol component being methyl 5-hydroxymethyl-2-furoate **9**.

Experimental

General

The NMR spectra were recorded on a Jeol JNM - LA -400 FT instrument, with Me_4Si as internal standard. Mass spectra were recorded by Drs. Morris and Reidy in the Athlone Institute of Technology, Ireland, using a Shimadzu GC/MS QP 2000 instrument

1,1-*Bis* - (2′- *methoxyfuroyl*- 5′ - *methyleneoxy*) *methane* **5**

Treatment of methyl 2-furoate (63 g, 0.5 mol) in chloroform (125 cm^3) with dry hydrogen chloride, paraformaldehyde (21.5 g) and anhydrous zinc chloride (18.5 g) at 35°C for 3 h gave methyl 2-chloromethyl-5-furoate (57 g, 60%) bp 95 °C/1 mm which gave plates mp 33°C (Lit., [1] 33°C) on cooling. After distillation of the product, the residue solidified. Recrystallation from EtOH gave 1,1-bis (2′-methoxyfuroyl-5′-metheleneoxy) methane **5** (15.5 g, 9.6%) as glistening plates, mp 76–78°C (Found: C, 55.6; H, 4.51. $C_{15}H_{16}O_8$ requires C, 55.6; H, 4.94%); V_{max} (Nujol) 1731 (C = 0 ester), 1602, 1543 cm^{-1} (furan ring); δ_H ($CDC1_3$) 3.89 (6 H, s, s, 2 × OMe), 4.64 (4 H, s, 2 × OCH_2), 4.82 (2 H, s, OCH_2O), 6.49 (2 H, d, 4′-H) and 7.15 (2 H, d, 3′-H); δ_c 51.9 (CH_3O), 61.4 (OCH_2), 94.0 (OCH_2O), 111.2 (C-4′), 118.7 (C-3′), 144.5 (C-5′), 155.5 (C-2′), and 159.0 (C = O); *m/z* 324 (M^+, 43%), 165 (100%).

1,1-*Bis* - (2′- *carboxy* - 5′ - *furfuryloxy*) *methane* **6**

Ester **5** (3 g, 9.25 mmol) in aqueous sodium hydroxide (2M, 70 cm^3) and ethanol (2 cm^3) was heated at 90°C for 1 h. After cooling, the solution was neutralised with dilute sulphuric acid, and the product was extracted with ether. The extract was washed with water, dried over Na_2SO_4 and was evaporated under reduced pressure. The resulting solid was recrystallised from EtOH to give 1,1-bis (2′-carboxy-5′- furfuryloxy) methane **6** (2.08 g , 76%) as white prisms, mp. 204 - 206°C (Found: C, 53.0; H, 4.04. $C_{13}H_{12}O_8$ requires C, 52.7; H, 4.05%); V_{max} (Nujol) 3120 (furan ring), 2923 (O – H of acid), 1684 (C = O), 1537 and 1464 cm^{-1} (furan); δ_H [$(CD_3)_2$ SO] 4.57 (4 H, s, 2 × CH_2O), 4.75 (2 H, s, OCH_2O) 6.59 (2 H, d, 4′-H), 7.15 (2 H, d, 3′-H) and 13.9 (2 H, broad s, OH); δ_c 61.0 (CH_2O), 93.6 (OCH_2O), 111.5 (C-4′), 118.5 (C-3′), 144.9 (C-5′), 155.4 (C-2′), and 159.4 (C = O); *m/z* 207 (M^+ -89, 26%), 81 (100%).

Decarboxylation of 1,1-*Bis*(2′-*carboxy*-5′-*furfuryloxy*) *methane* **6**

Dicarboxylic acid **6** (0.75 g, 2.5 mmol), copper bronze (1 g) and quinoline (15 cm^3) were heated to 220 °C, when decarboxylaton proceeded smoothly. After liberation of the required volume of CO_2 (112 cm^3), the mixture was cooled and was extracted with ether. The extract was washed (dilute H_2SO_4, water, brine) and was dried (Na_2SO_4). Evaporation under reduced pressure gave a syrup which was chromatographed on silica gel with ether-light petroleum (b.p. 40–60°C) (10 : 1 v/v) as eluant. 1,1-*Bis*(2′-*furfuryloxy*) *methane* **7** was obtained as a golden syrup (0.33 g, 62%) (Found: C, 63.7; H, 5.91. $C_{11}H_{12}O_4$ requires C, 63.5; H, 5.77%); δ_H ($CDC1_3$) 4.57 (4 H, s 2 × CH_2O), 4.76 (2 H, s, OCH_2O), 6.34 (4 H, d, 3′-H and 5′-H), and 7.41 (2 H, t, 4′-H); δ_c 61.0 (CH_2O), 92.9 (OCH_2O), 109.5 (C-3′), 110.25 (C-4′), 142.9 (C-5′), and 151.2 (C-2′).

Synthesis of 1,1-*Bis*(2′-*furfuryloxy*) *methane* **7**

Sodium hydride (80% in oil, 3.9 g, 0.13 mol) was added over 30 min to furfuryl alcohol (10 cm^3, 0.12 mol) in N,N-dimethylformamide (150 cm^3) at 0°C. After stirring at room temperature for 1 h, the solution was re-cooled to 0°C and dibromomethane (4.1 cm^3, 0.6 mol) was added, while keeping the temperature below 25°C. The mixture was stirred at room temperature for 18 h, during which three further additions of dibromomethane (total, 1.4 cm^3, 20 mmol) and sodium hydride (0.6 g, 20 mmol) were made at 4 h intervals. The brown mixture was cooled to 0°C and methanol (20 cm^3) was added. Evaporation under reduced pressure gave a dark syrup, which was taken up in chloroform (150 cm^3). The solution was washed (water, brine), dried (Na_2SO_4) and evaporated to a dark syrup which was chromatographed on silica gel (120 g). Elution with dichloromethane gave 1,1-bis(2′-furfuryloxy)methane **7** as a golden syrup (8.7 g, 70%), identical with the product described above.

1,1-*Bis*(2′-*formyl*-5′-*furfuryloxy*) *methane* **8**

Phosphorous oxychloride (0.7 cm^3, 7.5 mmol) was added dropwise with stirring over 30 min to N,N-dimethylformamide (40 cm^3) at –5 °C. The mixture was kept at 0–5 °C for 40 min and 1,1,bis(2′-furfuryloxy) methane **7** (1.4 g 6.7 mmol) in N,N-dimethylformamide (20 cm^3) was added dropwise. After reaching room temperature the mixture was stirred for 18 h, and was then poured into ice-water (60 cm^3). Aqueous potassium carbonate (1.32 g in 50 cm^3, 9.5 mmol) was added; the mixture was stirred for 16 h, and was extracted with ether. The extract was washed with water (× 3) and with brine. After drying (Na_2SO_4), the solution was evaporated under reduced pressure. The resulting syrup was chromatographed on silica gel (150 g). Elution with dichloromethane-acetone (10: 1 v/v) gave 1,1,bis(2′-formyl-5′-furfuryloxy) methane **8** (0.5 g, 28%), as white crystals mp 51–53 °C (from EtOH) (Found: C, 58.8; H 4.25). $C_{13}H_{12}O_6$ requires C, 59.1; H, 4.58%); V_{max} (Nujol) 2924, 2854 (CHO), 1671 (C = O), 1528 and 1459 cm^{-1} (furan); δ_H($CDC1_3$), 4.56 (4 H, s, 2 × CH_2O), 4.74 (2 H, s, OCH_2O), 6.47 (2 H, d, 4′-H), 7.13 (2 H, d, 3′-H), and 9.51(2 H, s, CHO), δ_c 61.3, (CH_2O), 94.1 (OCH_2O), 111.4 (C-4′), 122.0 (C-3′), 152.5 (C-5′), 157.25 (C-2′), and 177.5 (CHO).

The formyl compound **8** was treated with 2,4-dinitrophenylhydrazine in methanol containing sulphuric acid and after chromatography on silica gel (dichloromethane as solvent) a 2,4-dinitrophenylhydrazone was obtained, red needles (from MeOH) mp 105 – 107 °C (Found: C, 48.3; H, 3.25; N, 17.5. $C_{25}H_{20}N_8O_{12}$ requires C, 48.1; H, 3.23, N, 17.9%);λ_{max} (in $CHC1_3$) 390 mμ (ε 25,700). The formyl compound **8** with buffered semicarbazide in aqueous ethanol gave a semicarbazone which was purified by chromatography on silica gel with dichloromethane-acetone (5 : 1 v/v) as solvent to give white plates (from EtOH), mp 210 – 212 °C (Found: C, 47.3; H, 4.73; N, 21.7. $C_{15}H_{18}N_6O_6$ requires C, 47.6; H, 4.80; N, 22.2%).

Oxidation of 1,1-*Bis*(2′-*formyl*-5′-*furfuryloxy*) *methane* **8**

To aqueous sodium hydroxide (2.5%, 100 cm^3), copper (I) oxide (1.2 g, 8.4 mmol) was added followed by aqueous silver nitrate (0.1 g in 15 cm^3, 0.59 mmol). The resulting dark brown suspension was heated to 55°C. Vigorous stirring was started and a rapid stream of oxygen was bubbled through, as the formyl compound **8** (2 g, 7.6 mmol) and aqueous sodium hydroxide (0.3 g in 20 cm^3, 7.6 mmol) were added simultaneously at such a rate as to maintain the temperature at 50–55°C. Stirring and passage of oxygen were continued for 4 h. The mixture was filtered and the filtrate was extracted with ether (3 × 30 cm^3). The extract was washed with water (× 3) and with brine. After drying (Na_2SO_4) the solution was evaporated under reduced pressure. The resulting solid was chromatographed on silica gel with dichloromethane-acetone (10:1 v/v) as eluant. 1,1,Bis(2′-carboxy-5′-furfuryloxy)methane **6** (1.67 g, 74%) was obtained as white prisms (from MeOH) mp and mixed mp 204–206 °C. The NMR spectroscopic data were identical to those obtained for the compound **6**, obtained as described above.

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