Studies on the Furan Series

Part II. Oxidation of Bis(5-methoxycarbonyl-2-furyl)methane

SEppo PENNANEN

Department of Chemistry, Helsinki University of Technology, Otaniemi, Finland

Bis(5-methoxycarbonyl-2-furyl)methane, having electron withdrawing substituents in the furan rings, can easily be oxidized to the corresponding ketone. The reaction on methyl 2-furoate with carbon tetrachloride in the presence of AlCl₃ did not give the expected ketone, but tris(5-methoxycarbonyl-2-furyl)carbinol (III). Some reactions of 2,2'-difurylketone derivatives are described.

A previous paper¹ describes the condensation of methyl 2-furoate with trioxane in concentrated sulphuric acid, which gives bis(5-methoxycarbonyl-2-furyl)methane (I). The methylene group in compound I has properties similar to those of the corresponding group in diphenylmethane. Compound I is smoothly oxidized with CrO₃ in refluxing glacial acetic acid to bis(5-methoxycarbonyl-2-furyl)ketone (II) in 62% yield (Scheme 1).

\[ \text{Scheme 1.} \]

The electron withdrawing methoxycarbonyl groups in the furan rings stabilize compound II to withstand the strong oxidation conditions.

An attempt to synthesize compound II via the reaction of methyl 2-furoate with CCl₄ in the presence of AlCl₃ (analogous to the preparation of benzophenone from benzene and CCl₄/AlCl₃) gave no II. However, another compound was obtained, which had \( \nu \) 3340 cm⁻¹ in the IR spectrum due to a hydroxyl group. This could not be acetylated, but silylation with Me₃SiCl produced a trimethylsilyl ether. According to the mass spectrum the molecular weight of the hydroxyl product was 404. The formula tris(5-methoxycarbonyl-

Acta Chem. Scand. 26 (1972) No. 5
2-furyl)carbinol (III) was indicated for this compound by the spectra and elemental analyses.

The fact that the reaction (Scheme 2) gave only III but no II is explained by the great reactivity of the furfuryl chloride intermediate. Kirner has mentioned that furfuryl chloride is 1500 times more reactive than benzyl chloride. While the reaction of benzene and CCl₄/AlCl₃ stops at the stage of the diphenyl dichloromethane/AlCl₃ complex (which is hydrolyzed to benzophenone), the analogous complex (now reactive) from the furanoid compound and CCl₄/AlCl₃ reacts once more with a molecule of methyl 2-furoate to give the trifurylchloromethane/AlCl₃ complex. (Scheme 2).

\[
\begin{align*}
3 \times \begin{array}{c}
\text{O} \\
\text{OMe}
\end{array} & \xrightarrow{\text{AlCl₃}} \begin{array}{c}
\text{O} \\
\text{OMe}
\end{array} \\
& \xrightarrow{\text{H₂O}} \begin{array}{c}
\text{O} \\
\text{COH}
\end{array}
\end{align*}
\]

\textit{Scheme 2.}

Compound III, like the triarylcarihinoils, forms a bright red halochromic salt with strong acids (e.g., conc. H₂SO₄). Ramanathan and Levine have mentioned that difurylcarbinols and related compounds are quite sensitive to oxygen, and when exposed to air are oxidized to black resins. The stability of III towards air and conc. H₂SO₄ is due to the electron-withdrawing ester groups in the three furan rings.

Some reactions of bis(5-methoxycarbonyl-2-furyl)ketone. II is hydrolyzed with KOH in methanol into bis(5-carboxy-2-furyl)ketone (IV), m.p. > 310°C. The dicarboxylic acid IV can be decarboxylated with copper in quinoline at 150–160°C to 2,2'-difurylketone (V). Reichstein et al. have previously prepared V by the Grignard reaction of 2-bromofuran and 2-cyanofuran. Boyle et al. and Michael and Hörnfeldt have treated 2-furyllithium with gaseous carbon dioxide and dimethylcarbamoyl chloride, respectively, to give V.

The reduction of II with NaBH₄ gave bis(5-methoxycarbonyl-2-furyl)carbinol (VI) in quantitative yield.

The ketone group of II is to some extent sterically hindered, because no phenylhydrazine adduct was formed.

Baeyer-Villiger conditions (40 % peracetic acid) failed to affect II. However, oxime (VII) was formed after 65 h refluxing in dried dioxane. The Beckmann rearrangement of the oxime VII was attempted by the methods of Hill and Chortyk and Emmons (or concentrated sulphuric acid at 80°C) but no reaction took place. When the temperature of the conc. H₂SO₄ was 100–110°C, sulphonation of the furan rings probably occurred because the compound became water soluble.

In contrast to the failure of the Baeyer-Villiger reaction and the Beckmann rearrangement, the Schmidt reaction was successful. When II was treated with sodium azide in polyphosphoric acid, the compound formed was, according to the spectra and elemental analyses, N-(5-methoxycarbonyl-2-furyl)-5-methoxycarbonyl-2-furamide (VIII). Because the ketone II is symmetrical, only one rearrangement product resulted.

\textit{Acta Chem. Scand. 26 (1972) No. 5}
Scheme 3. Some reactions of bis(5-methoxycarbonyl-2-furyl)ketone.

White\textsuperscript{12} has mentioned that when $N$-alkylamide, under cooling, is treated with nitrogen tetroxide, the result is a labile $N$-alkyl-$N$-nitrosoamide which can be rearranged by heating to an ester or an acid and an alkene. When VIII was treated at $-70^\circ C$ with $N_2O_4$ and after that refluxed in $CCl_4$, 2,5-furandicarboxylic acid monomethyl ester (X) was produced. According to the mechanism proposed by White,\textsuperscript{12} the formation of compound X can be visualized as given in Scheme 4.

Scheme 4.

\textit{Acta Chem. Scand.} 26 (1972) No. 5
EXPERIMENTAL

The spectra were determined on the following instruments: NMR spectra on a Varian A60, UV spectra on a Beckman DK-2, IR spectra on a Perkin-Elmer 257B, and mass spectra on a Perkin-Elmer 270B. Elemental analyses were carried out on an F&M 185 CHN-analyzer. All melting points are uncorrected.

The preparation of the starting material bis(5-methoxy carbonyl-2-furyl)methane (I) is described in the previous paper.¹

**Bis(5-methoxy carbonyl-2-furyl)ketone (II).** 2.60 g of I and 5.20 g of K₂Cr₂O₇ were refluxed in 70 ml of glacial acetic acid for 5 h. The mixture was cooled and poured into 400 ml of cold water. The precipitate formed was filtered, washed first with dilute HCl, bichromate solution and after that with ethyl acetate. The recrystallization of the greyish material was performed in water-acetic acid mixture. Yield 1.70 g (62 %); m.p. 205–206°C; λₘₐₓ 313 (ε 26 000), 322 (ε 25 800) nm; rₘₐₓ 3160, 2960, 1720, 1630 cm⁻¹; 1H (in CF₃COOH) 2.37 (2H d 3.5 cps), 2.74 (2H d 3.5 cps), 6.18 (6H s). (Found: C 56.09; H 3.56. Calc. for C₅H₆O₂: C 56.12; H 3.62.)

**Tria(5-methoxy carbonyl-2-furyl)carbinol (III).** 5.00 g of methyl 2-furoate and 10.00 g of AlCl₃ were refluxed in 100 ml of CCl₄ for half an hour. The reaction mixture was poured into ice water, which was extracted with two portions (75 ml) of ethyl acetate. The ester layer was separated, dried with MgSO₄ and evaporated. The brown, viscous residue was purified by silica gel column chromatography (elution with EtOAc–CHCl₃ 1:1). The recrystallization was carried out in a mixture of petrol ether and chloroform. Yield 1.30 g (25 %); m.p. 147°C; λₘₐₓ 260 (ε 26 700) nm; rₘₐₓ 3340, 3130, 2950, 1730, 1065 cm⁻¹; 1H (in acetone) 2.78 (3H d 3.5 cps), 3.43 (3H d 3.5 cps), 3.28 (1H s dis. with D₂O), 6.18 (9H s); m/e 404 (26 %), 387 (100 %), 373 (12 %), 345 (37 %). (Found: C 56.53; H 3.75. Calc. for C₉H₁₀O₂: C 56.44; H 3.98.) Acetylation of III did not succeed. Silylation of III was carried out with trimethylchlorosilane in triethylamine. The NMR spectrum of the silyl ether: τ 2.92 (3H d 3.5 cps), 3.58 (3H d 3.5 cps), 6.19 (9H s), 9.98 (9H s).

**Bis(5-carboxy-2-furyl)ketone (IV).** 10.00 g of II was kept with 8.00 g of KOH in 150 ml of water–methanol (1:10) for 12 h at room temperature. The mixture was acidified with HCl and the precipitate formed was separated, washed with water and dried. Yield 7.80 g (97 %); m.p. > 310°C; rₘₐₓ 3400–2500 (broad) cm⁻¹.

2,2’-Difurylketone (V). 2.00 g of IV and 0.50 g of finely powdered copper in 30 ml of quinoline were stirred at 150–160°C for 2 h. After cooling, 100 ml of ethyl acetate was added and quinoline was washed off with dilute HCl. The organic layer was then washed with water, dried with MgSO₄ and evaporated. The residue (almost black, viscous oil) was purified in a silica gel column (elution with chloroform). Yield 1.10 g (95 %); m.p. 32°C (recryst. from petrol ether). Reichenstein et al.⁴ give the melting point as 33–34°C. rₘₐₓ 3134, 1630, 1500, 870 cm⁻¹; τ 2.34 (2H d 1.5 cps), 2.54 (2H d 3.5 cps), 3.45 (2H dd 1.5 and 3.5 cps).

**Bis(5-methoxy carbonyl-2-furyl)carbinol (VI).** 2.00 g of II and 0.40 g of NaN₃ were refluxed in 40 ml of CHCl₃ for 4 h. The mixture was washed with water, dried with MgSO₄ and evaporated. The residue was recrystallized from a mixture of petrol ether and CHCl₃. Yield 2.00 g (99 %); m.p. 144°C; rₘₐₓ 3578, 3125, 2960, 1725; 1H (in CDCl₃) 2.87 (2H d 3.5 cps), 3.52 (2H d 3.5 cps), 4.08 (1H s), 4.11 (1H s dis. with D₂O), 6.12 (6H s). (Found: C 55.45; H 4.41. Calc. for C₉H₁₀N₂O₂: C 55.72; H 4.32.)

**Bis(5-methoxy carbonyl-2-furyl)ketone oxime (VII).** 1.50 g of II, 5 ml of dry pyridine, and 1.50 g of NH₄OH.HCl were refluxed in dried dioxane for 65 h. The mixture was poured into water. The precipitate formed was washed with water and recrystallized from ethanol. Yield 1.40 g (89 %); m.p. 216°C; λₘₐₓ 286 (ε 35 200) nm; rₘₐₓ 3360, 3160, 2960, 1730, 1690, 990 cm⁻¹; 1H (in C₂H₅COOH) 2.11 (2H d 3.5 cps), 2.48 (2H d 3.5 cps), 5.90 (6H s). (Found: C 53.11; H 3.87; N 4.56. Calc. for C₉H₆N₂O₂: C 53.24; H 3.78; N 4.78.)

N-(5-Methoxy carbonyl-2-furyl)-5-methoxy carbonyl-2-furamide (VIII). 1.00 g of II was heated in PPA at 75°C. 0.30 g of NaN₃ was added gradually. After 3 h the mixture was poured into water, which was extracted twice with 50 ml of EtOAc. The organic layer was washed with water, dried with MgSO₄ and evaporated. The brownish residue was purified in a silica gel column (elution with CHCl₃–EtOAc 1:1). Yield 0.65 g (62 %); m.p. 223°C (recryst. from ethanol); λₘₐₓ 262 (ε 31 500), 311 (ε 33 100) nm; rₘₐₓ 3300, 3150, 2950, 1720, 1675, 1540, 1520 cm⁻¹; 1H (in acetone) 2.73 (2H d 3.5 cps), 3.28 (2H d...
STUDIES ON THE FURAN SERIES II 1965

3.5 cps), 6.01 (3H s), 6.08 (3H s). (Found: C 53.18; H 3.65; N 4.77. Calc. for C₁₀H₁₁O₇: C 53.24; H 3.78; N 4.78.)

N-Nitroso-N-(5-methoxycarbonyl-2-furyl)-5-methoxycarbonyl-2-furamide (IX) and 2,5-furandicarboxylic acid monomethylester (X). 0.30 g of VII in 40 ml of EtOAc was treated with 3 ml of liquid N₂O₄ at −70°C. The mixture was stirred and its temperature rose to 20°C during 2 h. Water was added; the organic layer was dried with MgSO₄ and evaporated. The residue (the labile N'-nitroso compound IX) was not purified, but dissolved in 50 ml of CCl₄ and refluxed for 12 h. CCl₄ was evaporated and the black residue was purified in a silica gel column (elution EtOAc–AcOH 10 : 1). Yield 0.12 g (82 %) of X; m.p. 198°C (recryst. from hot water). Ref. 13 gives the m.p. as 201°C. v_max 3200 – 2500, 1720, 1690 cm⁻¹; τ (in CF₃COOH) 2.58 (1H d 4 cps), 2.62 (1H d 4 cps), 5.95 (3H s). The color reaction with isatine 13 to confirm 2,5-furandicarboxylic acid gave positive result when hydrolyzed X was used.

Acknowledgements. The author is greatly indebted to Professor G. Nyman for his interest in this work. Thanks are due to Associate Professor J. Gripenberg and T. Hase, Ph.D., for fruitful discussions and comments. Financial support from Neste Oy:n Säätiö is gratefully acknowledged.

REFERENCES


Received September 21, 1971.

Acta Chem. Scand. 26 (1972) No. 5