

# Synthesis of Tetra-substituted Furan Derivatives from 1-Arylpropane-2,3-diones

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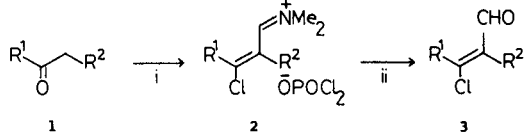
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1-Arylpropane-2,3-diones **4** gave 2-dimethylamino-3-formyl-4-chloro-5-arylfuran derivatives **7** in the Vilsmeier reaction.

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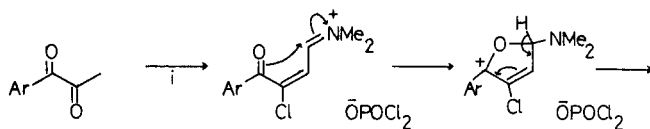
When ketones **1** are reacted under Vilsmeier conditions [1], 2-chlorovinylaldehyde derivatives **3** are obtained (Scheme 1) after hydrolysis of the intermediate iminium salts **2** [2]. We were interested in extending the Vilsmeier reaction of ketones to include 1,2-diketones and we report that 1-arylpropane-2,3-diones **4** yielded 2-dimethylamino-3-formyl-4-chloro-5-arylfuran derivatives **7** under Vilsmeier conditions (Scheme 2). The mechanisms proposed for the formation of aldehydes **7** from diones **4** and aldehydes **3** from ketones **1** are closely related because in both cases enolisable carbonyl groups are transformed into 2-chlorovinyliminium salts **2** or **5** by the action of a mixture of dimethylformamide (DMF) and phosphorus oxychloride. In the case of iminium salts **5** an intramolecular cyclisation gives furans **6** which undergo a further Vilsmeier reaction affording, after hydrolysis, aldehydes **7**.

Scheme 1



Reagents: i,  $\text{POCl}_3/\text{DMF}$ ; ii, hydrolysis

Scheme 2

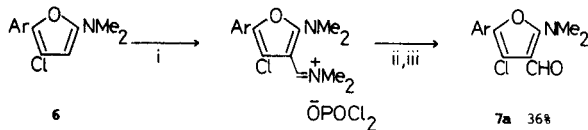


**4a** Ar = phenyl

**4b** Ar = 4-chlorophenyl

**4c** Ar = 4-methoxyphenyl

**4d** Ar = 4-hydroxyphenyl



**7a** 36%

**7b** 28%

**7c** 36%

**7d** 15%

Reagents: i,  $\text{POCl}_3/\text{DMF}$ ; ii,  $\text{NaClO}_4/\text{H}_2\text{O}$ ; iii,  $\text{H}_2\text{O}/\text{OH}^-/\text{EtOH}$

Many aromatic heterocyclic and carbocyclic ring systems have been prepared by application of the Vilsmeier reaction to acyclic precursors [3] and our investigations provide a novel method for synthesising furan derivatives **7**.

## EXPERIMENTAL

Proton-nmr were determined at 270 MHz using tetramethylsilane as an internal standard. Infra-red spectra were recorded as potassium bromide discs.

### 2-Dimethylamino-3-formyl-4-chloro-5-phenylfuran (**7a**).

To DMF (30 ml) was added phosphorus oxychloride (24.5 g) dropwise with cooling (ice-bath). The mixture was allowed to stand (0.5 hour) and 1-phenylpropane-2,3-dione (**4a**) (6.0 g) was then added dropwise (5 minutes). The mixture was heated (1 hour) at  $90^\circ$ , allowed to cool to room temperature and then poured onto ice and excess sodium perchlorate. The resulting brown perchlorate salt was collected, washed several times with water, suspended in methanol (20 ml) and re-filtered. After washing with methanol (2 x 10 ml) and then ether the bright yellow solid (7.6 g) was added to aqueous ethanolic sodium hydroxide solution. The mixture was poured into water giving furan **7a** (4.5 g) as a tan solid. Recrystallisation from methanol afforded fine white needles (3.6 g, 36%), mp  $91-92^\circ$ ; ir: 1885, 1670, 1620, 1580,  $1400\text{ cm}^{-1}$ ;  $^1\text{H-nmr}$  (acetone- $d_6$ ):  $\delta$  9.61 (1H, s, CHO), 7.82 (2H, d,  $J = 8\text{ Hz}$ , PhH), 7.46 (2H, t,  $J = 8\text{ Hz}$ , PhH), 7.30 (1H, m, PhH), 3.35 ppm (6H, s,  $\text{NMe}_2$ ).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{12}\text{ClNO}_2$ : C, 62.5; H, 4.8; Cl, 14.2; N, 5.6. Found: C, 62.6; H, 4.8; Cl, 14.2; N, 5.4.

By a similar procedure the following furans **7** were prepared.

### 2-Dimethylamino-3-formyl-4-chloro-5-(4-chlorophenyl)furan (**7b**).

DMF (20 ml), phosphorus oxychloride (6.1 g) and 1-(4-chlorophenyl)propane-2,3-dione (**4b**) [4] (1.8 g) yielded furan **7b** (0.8 g, 28%) as tan needles, mp  $120-121^\circ$  after recrystallisation from methanol; ir: 1885, 1670 (weak), 1630, 1610, 1600, 1410,  $1395\text{ cm}^{-1}$ ;  $^1\text{H-nmr}$  (acetone- $d_6$ ):  $\delta$  9.60 (1H, s, CHO), 7.83 (2H, d,  $J = 8\text{ Hz}$ , ArH), 7.47 (2H, d,  $J = 8\text{ Hz}$ , ArH), 3.36 ppm (6H, s,  $\text{NMe}_2$ ).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{11}\text{Cl}_2\text{NO}_2$ : C, 54.9; H, 3.9; Cl, 25.0; N, 4.9. Found: C, 55.1; H, 3.9; Cl, 25.0; N, 4.8.

### 2-Dimethylamino-3-formyl-4-chloro-5-(4-methoxyphenyl)furan (**7c**).

DMF (15 ml), phosphorus oxychloride (6.1 g) and 1-(4-methoxyphenyl)propane-2,3-dione (**4c**) [4] (1.8 g) yielded furan (**7c**) (1.0 g 36%) as cream needles, mp  $78-79^\circ$  after recrystallisation from methanol; ir: 1670, 1575, 1510, 1415, 1400,  $1250\text{ cm}^{-1}$ ;  $^1\text{H-nmr}$  (deuteriochloroform):  $\delta$  9.59 (1H, s, CHO), 7.72 (2H, d,  $J = 9\text{ Hz}$ ,

ArH), 6.95 (2H, d, J = 9 Hz, ArH), 3.84 (3H, s, OMe), 3.31 ppm (6H, s, NMe<sub>2</sub>).

*Anal.* Calcd. for C<sub>14</sub>H<sub>14</sub>ClNO<sub>3</sub>: C, 60.1; H, 5.1; Cl, 12.7; N, 5.1. Found: C, 60.2; H, 5.0; Cl, 12.8; N, 4.9.

2-Dimethylamino-3-formyl-4-chloro-5-(4-hydroxyphenyl)furan (**7d**).

DMF (15 ml), phosphorus oxychloride (7.6 g) and 1-(4-hydroxyphenyl)propane-2,3-dione (**4d**) [5] (1.6 g) yielded furan (**7d**) (0.4 g, 15%) as tan needles, mp 184° dec after recrystallisation from methanol; ir: 3450, 1660, 1560, 1515, 1380, 1280 cm<sup>-1</sup>; <sup>1</sup>H-nmr (dimethylformamide-d<sub>7</sub>): δ 9.61 (1H, s, CHO), 7.70 (2H, d, J = 9 Hz, ArH), 6.97 (2H, d, J = 9 Hz, ArH), 3.35 ppm (6H, s, NMe<sub>2</sub>).

*Anal.* Calcd. for C<sub>13</sub>H<sub>12</sub>ClNO<sub>3</sub>: C, 58.5; H, 4.6; Cl, 13.3; N, 5.3. Found: C, 58.5; H, 4.6; Cl, 13.2; N, 5.1.

## REFERENCES AND NOTES

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