

Synthesis of 5,5'-Diformyl-2,2'-difuran from 2-Furfural by Photochemical Aryl Coupling

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Dedicated to Emeritus Professor A. Goosen, the optimist who taught us.

Abstract: The synthesis of 5,5'-diformyl-2,2'-difuran (IUPAC name: [2,2'-bifuryl]-5,5'-dicarbaldehyde) in good yields by the intermolecular coupling of 2-furfural and 5-bromo-2-furfural has been achieved. Optimum yields were obtained when mixtures of the substrates in acetonitrile were treated with polyvinylpyridine powder (Reillex 402), and irradiated with UV light through a quartz filter. Low yields of

coupling product were obtained in the absence of this base or if hydrocarbon solvents were used. A mechanistic pathway involving a transient exciplex intermediate has been proposed.

Keywords: aldehydes; aryl coupling; difurans; 2-furfural; oxygen heterocyclics; photochemistry; polyvinylpyridine

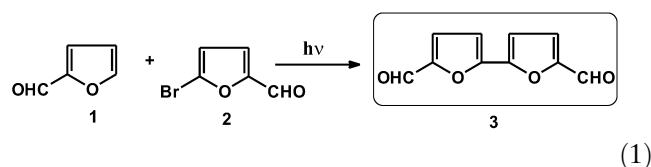
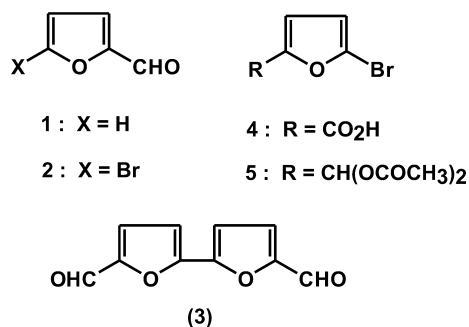
Introduction

As part of our investigations into the chemistry of 2-furfural and its derivatives, a supply of 5,5'-diformyl-2,2'-difuran **3** was needed. This compound had previously been obtained either through an Ullmann condensation utilising 5-iodo-2-furfural,^[1] Pd-catalysed coupling of 2-furfural **1**,^[2] or *via* the photolytic dimerisation of 5-bromo-2-furfural **2**.^[3] The photolytic substitution of 3- and 5-halogenated-2-furyl derivatives in aromatic solvents was reported to give good yields of the corresponding 3- and 5-aryl derivatives.^[4] However, reports on the photochemical aryl coupling reactions of 5-bromo-2-furfural **2** with other derivatives are limited.^[5] Most of the reported syntheses of the target compound involve laborious work-up steps, high cost and gave low yields. Thus the photochemical coupling reaction seemed a very attractive route to **3** and we

report on the reaction conditions for the efficient coupling of 5-bromo-2-furfural **2** with 2-furfural **1** in the presence of a polymeric base, producing **3** in good yields.

Results and Discussion

The photolysis of 2-furfural **1** in acetonitrile with UV light through a quartz filter for 24 h, surprisingly, gave only starting and polymeric material. However, irradiation of a 1:1 molar equivalent ratio of 2-furfural **1** and 5-bromo-2-furfural **2** in the presence of a polyvinylpyridine catalyst (Reillex 402) under the same conditions gave 87% of 5,5'-diformyl-2,2'-difuran **3** on isolation, after separation of the reaction components (Table 1, entry 3, Eq. 1). In the absence of base, only 7% of the dimer **3** could be isolated (Table 1, entry 1).



Changing the solvent to either petroleum ether or hexane led to a decrease in the conversion of starting material over the same time interval with a concomitant

Table 1. Photochemical synthesis of 5,5'-diformyl-2,2'-difuran **3**.

Entry	2-Furfural 1 [mol equiv.] ^[a]	Solvent	Time [h]	Conversion [%]	Yield [%] ^[b]
1	1	CH ₃ CN	24	20	7 ^[c, d]
2	0	CH ₃ CN	16	100	82
3	1	CH ₃ CN	24	100	87
4	1	Pet. Ether	24	30	20
5	1	CH ₂ Cl ₂	24	20	10
6	1	<i>n</i> -hexane	24	20	5
7	4	CH ₃ CN	24	100	60 ^[d]
8	6	CH ₃ CN	10	100	82 ^[d]
9	20	CH ₃ CN	24	100	81 ^[d]
10	20	CH ₃ CN	24	10	0 ^[d, e]
11	20	Pet. Ether	24	10	0 ^[d, e]
12	20	CH ₃ CN	35 days	100	76 ^[d, e]

^[a] 5-Bromo-2-furfural **2** (1 mol. equiv.) in the presence of Reillex 402 (0.4 g), see experimental section.

^[b] Isolated yields based on **2**.

^[c] No Reillex present.

^[d] Black polymeric material formed as by-product.

^[e] Irradiated through a Pyrex filter-all other irradiations through quartz.

decrease in the yields of dimer **3** (20% and 5%, respectively; entries 4 and 6 in Table 1). Dichloromethane had an even more deleterious effect on both the conversion of **1** and yield of **3** due to the formation of copious amounts of black polymeric material, which not only screened off the UV radiation, but also complicated the isolation of the product (Table 1, entry 5). The solvent is suspected to produce hydrogen chloride on irradiation,^[6] which in turn may induce the well-documented acid-catalysed polymerisation of furan derivatives.^[7]

Increasing the ratio of 2-furfural to 5-bromo-2-furfural (Table 1, entries 7–9), resulted in good yields of dimer **3**, the lower yield (entry 7), accompanied by copious quantities of black insoluble polymeric material. Irradiation through a Pyrex filter also gave no dimer and negligible conversion of starting materials was observed (entries 10 and 11). However, a good yield of **3** was obtained when a 20:1 ratio of 2-furfural to the 5-bromo derivative in acetonitrile contained in a Pyrex flask, was exposed to direct sunlight for 35 days (entry 12).

Acceptable yields of **3** were obtained even when a high 2-furfural to 5-bromo-2-furfural ratio were used, which renders the process more economically viable. 2-Furfural, a bulk chemical, is relatively cheap,^[8] whereas the other precursor **2** is obtained by the bromination of 2-furfural (*ca.* 50% yield), rendering it more expensive.

In an attempt to extend the scope of the reaction, photolysis of 5-bromo-2-furoic acid **4** and 5-bromofurilidene diacetate **5**, respectively, in the presence of 2-furfural **1** resulted in quantitative recovery of the starting materials.

D'Auria and D'Onofrio^[9] reported the aldehyde **1** to contain an impurity, which was suggested to effectively quench the excited state of the aldehyde molecule, forming an excited triplet state with high quantum yield phosphorescence. In order to eliminate similar impurities, which may possibly inhibit this homonuclear coupling reaction, furfural was converted to the diacetate with acetic anhydride in acetic acid. After crystallisation of the diacetate, the latter was hydrolysed back to the aldehyde, which was subsequently carefully redistilled in an inert atmosphere. Furfural purified by this method however, still resisted photocoupling.

The coupling reactions of 2-furfural and 5-bromo-2-furfural under irradiation were also monitored by HPLC (Figure 1). In the coupling reactions, the 5-bromo-2-furfural **2** disappeared at a faster rate than furfural **1**, suggesting that the bromo derivative initially couples to give **3** which then subsequently sensitises the reaction (Table 1, entry 2). Photolysis of furfural in the presence of added difurfural **3**, however, did not promote the coupling reaction significantly. In duplicate experiments, where the rate profiles were monitored by HPLC using reagents **1** and **2** in molar ratios of 20:1, 6:1 and 4:1, respectively, in the presence of Reillex, the bromide **2** disappeared at a much faster rate than the aldehyde **1** and is used up before the completion of the reaction, suggesting further production of the product **3** by direct sensitised coupling of 2-furfural **1**.

The presence of a small amount of a polyvinylpyridine (Reillex 402),^[10] as base was found to promote the coupling reaction, most probably by inhibiting acid-catalysed polymerisation of **1** which is suspected to be the main cause of the low yields of dimer **3** (Figure 1).

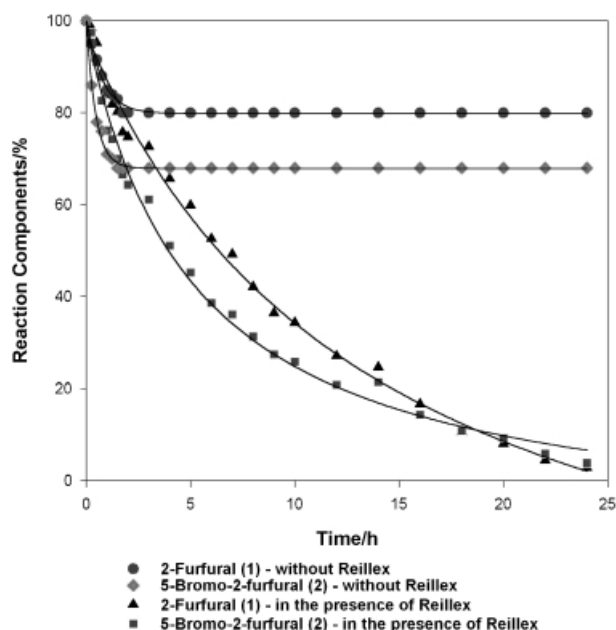
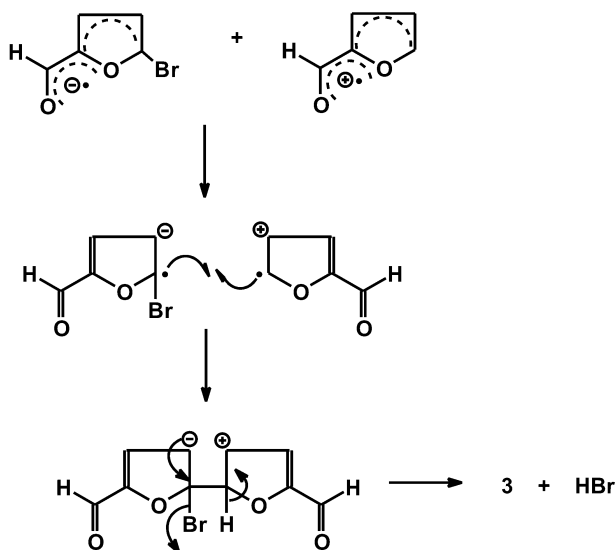


Figure 1. Photolysis of equimolar ratios of 2-furfural (**1**) and 5-bromo-2-furfural (**2**).

Although the exact nature of the mechanism for dimer formation is obscure at this stage, the exciplex pathway as proposed by D'Auria et al.^[11] for the photolytic coupling of 2-iodo-5-furfural with various aromatics seems to be an attractive possible pathway, especially in view of the well-known facile photochemical generation of radical-anions of thiophene-2-carbaldehyde.^[2]

Such a transient exciplex would also explain the regioselectivity observed in our photochemical coupling experiments of **1** and **2** (Scheme 1).^[11]



Scheme 1. A proposed mechanism for the photochemical coupling of **1** and **2**.

Conclusions

The photochemical synthesis of 5,5'-diformyl-2,2'-difuran **3** outlined above thus far constitutes the most efficient route to this product reported in the chemical literature, the reported synthesis has subsequently been performed successfully on a pilot-plant scale, and has been patented.^[14] The synthesis has the additional advantage in that it utilises relatively cheap starting materials and the polymeric base may easily be removed from the reaction product by simple filtration.

Experimental Section

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Elemental micro-analysis were performed in the micro-analytical laboratories of the University of Port Elizabeth. Low resolution mass spectra (EI; 70 eV) were determined on a Hewlett-Packard model 2648A instrument at the University of Port Elizabeth and high resolution mass spectra were performed on a Kratos double focusing instrument (Cape Technikon Mass Spectrometry Unit, Cape Town, South Africa). Infrared spectra were recorded on a Perkin-Elmer infrared Spectrometer, Model 1600 FTIR. 200 MHz ¹H NMR and ¹³C NMR spectra at 50 MHz were recorded in either CDCl₃ or DMSO-*d*₆ on a Varian Gemini 200 spectrometer with TMS as internal standard. Analytical HPLC was performed on a Waters 441 instrument equipped with a UV detector (254 nm) and a reversed phase C₁₈ radial-pak cartridge housed in a Waters RCH 8 × 10 module. The elution times of the reaction components, using acetonitrile/water (35/65 v/v) as mobile phase at a flow rate of 2.5 cm³ min⁻¹, are contained in Table 2.

Table 2. HPLC elution times for compounds **1**, **2** and **3**.

Compound	Elution Time [min]
2-Furfural 1	1.89
5,5'-Diformyl-2,2'-difuran 3	2.97
5-Bromo-2-furfural 2	3.72

Starting Materials

5-Bromo-2-furfural **2** was prepared from 2-furfural by bromination with bromine in 1,2-dichloroethane according to a published procedure.^[13] 2-Furfural **1** was distilled and analytical grade acetonitrile dried over molecular sieves prior to use. Reillex 402 (polyvinylpyridine)^[10] was activated by saturation with acetonitrile before use.

Photolytic Synthesis of 5,5'-Diformyl-2,2'-difuran **3**; General Procedure

5-Bromo-2-furfural **2** (2.0 g, 11.5 mmol) and 2-furfural **1** (1.1 g, 4.6 mmol) dissolved in acetonitrile (400 mL) contained in a quartz flask, were treated with activated Reillex 402 (0.4 g).

The solution was purged with dinitrogen for 15 min and then irradiated with a 450 W medium pressure Hanovia UV lamp at ambient temperature for 25 h. The solution was treated with activated charcoal (2 g) and warmed at 75 °C with stirring for 5 min, filtered while hot, concentrated under reduced pressure to a small volume (ca. 20 mL) and cooled to 0 °C for 20 min to afford light brown crystals of 5,5'-diformyl-2,2'-bifuran **3**; yield: 1.88 g (86.5%), mp 264–265 °C (lit.,^[12] mp 262–265 °C); IR (CHCl₃): ν_{max} = 1670 cm⁻¹ (s, CO); ¹H NMR (DMSO-*d*₆, 200 MHz): δ = 7.22 (2H, d, *J* = 3.9 Hz), 7.59 (2H, d, *J* = 3.9 Hz), 9.73 (2H, s, CHO); HRMS: *m/z* = 190.02753 (M⁺, 100%), 162.03197 (C₉H₆O₃, 5.99%), 161.02562 (C₉H₅O₃, 4.39%), 133.02886 (C₈H₅O₂, 50.32%), 105.03368 (C₇H₅O, 11.65%), 75.97654, 57.97654, 51.02352; C₁₀H₆O₄ requires: M⁺, 190.02661. Calcd. for C₁₀H₆O₄: C 63.16, H 3.18%; found: C 63.45, H 3.40%.

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