

Studies on the Furan Series

Part V. The Reaction of Furoin and Related Compounds with Vilsmeier Reagents. A Convenient Synthesis of Unsymmetrically 5,5'-Disubstituted Difurylethylene Derivatives

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The reaction of furoin (I) with DMF/POCl₃ complex gave both 5-chlorofurfuryl 2'-furyl ketone (II) and 5-formyl-2,2'-furyl (III). Under similar conditions thenoin (IV) and benzoin (V) produced α -chloro-2-thienyl 2'-thienyl ketone (VI) and α -chlorobenzyl phenyl ketone (VII), respectively. The diol (IX) obtained by the reduction of furoin gave smoothly (*E*)-1-(5-chloro-2-furyl)-2-(5-formyl-2-furyl)ethene (X) with the DMF/POCl₃ treatment. Analogously 1,2-di(2-thienyl)ethane-diol (XI) gave (*E*)-1-(5-chloro-2-thienyl)-2-(2-thienyl)ethene (XII), but 1,2-diphenylethanediol (XIII) gave 1,2-diphenylethanediol diformate (XIV). X was photocyclized to 7-chlorobenzo[1,2-b:4,3-b']-difuran-2-carboxaldehyde (XVIII).

Some unsuccessful attempts to synthesize furohelicenes from the derivatives of X and XVIII are described.

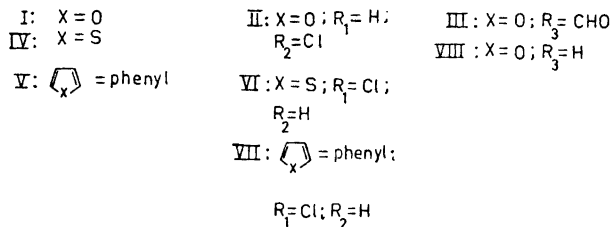
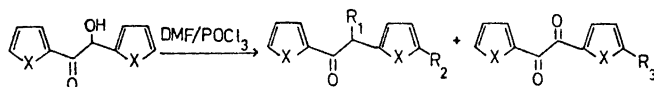
Numerous reactions of DMF complexes have been reported and reviewed.¹ In this work some new pathways in the reactions of Vilsmeier reagents are observed.

When furoin (I), easily obtainable from furfural, was treated with DMF/POCl₃ (1:1) complex in refluxing methylene chloride, the reaction gave no expected products, but 34 % of 5-chlorofurfuryl 2'-furyl ketone (II) and 26 % of 5-formyl-2,2'-furyl (III). It seems likely that two competing reactions, leading to II and III, are involved, as the amount of complex used had no noticeable effect on the ratio of yields. On the other hand, other DMF complexes caused a different distribution of products. DMF/COCl₂ and DMF/SOCl₂ gave 47 % of III (traces of II) and 54 % of II (traces of III), respectively (Scheme 1).

Compounds analogous to I, thenoin (IV) and benzoin (V), reacted with DMF/POCl₃ complex giving α -chloro-2-thienyl 2'-thienyl ketone (VI) and α -chlorobenzyl phenyl ketone (VII) (Scheme 1).

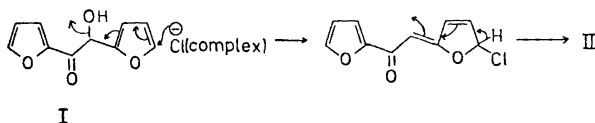
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Scheme 1.

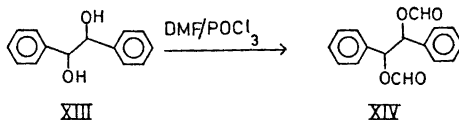
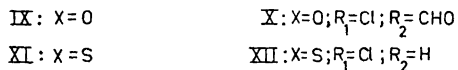
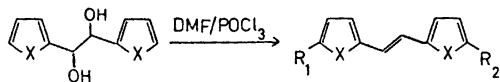
The formation of II can be considered as a substitution, where the chloride anion of the complex interacts with the hydroxyl group of furin:



Scheme 2.

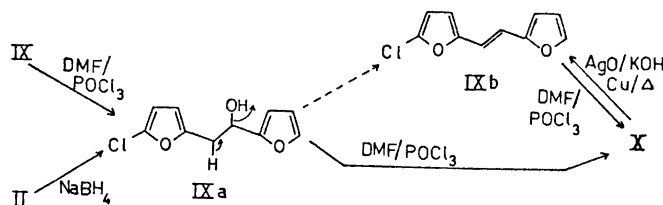
The compound III cannot be synthesized directly from furil (VIII) with the Vilsmeier reagent. Therefore it seems likely that formylation takes place on the furfuryl alcohol side of I followed by aerial oxidation of the alcohol. This is supported by the fact that under a nitrogen atmosphere no III is formed (only traces of II).

When I was reduced to the vicinal diol (IX) and treated with the Vilsmeier complex, only one yellow compound was produced and identified by spectral data as (*E*)-1-(5-chloro-2-furyl)-2-(5-formyl-2-furyl)ethene (X).

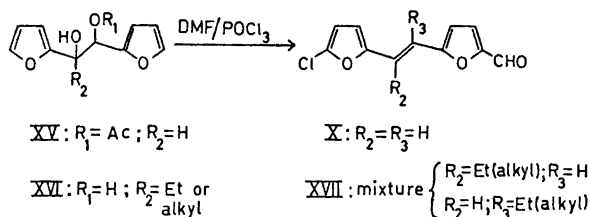


Scheme 3.

The reaction presumably starts with substitution, as the chlorinated compound IXa, obtainable from II by reduction, gives X, and continues with the elimination of water; as IXb, obtainable from X by oxidation and decarboxylation, similarly gives X (Scheme 4).



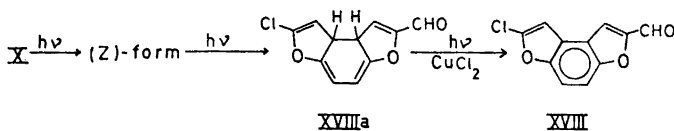
The reaction of the S-analogue (XI) of IX with DMF/POCl₃ stopped after substitution and elimination producing (*E*)-1-(5-chloro-2-thienyl)-2-(2-thienyl)-ethene (XII). The reaction with the benzenoid analogue, *vic*-1,2-diphenylethanedione (XIII), took quite another direction from that taken with IX and XI giving a normal esterification (diformylation) product: 1,2-diphenylethanedione diformate (XIV).



Some derivatives of IX were prepared (XV and XVI; Scheme 5) in order to see what effect the substituents might have on the reaction (Scheme 3). The compound XV gave X, as expected. XVI gave a mixture of two isomers. The alkyl substituents seem to have no directing effect on the reaction, as the NMR-spectrum of the mixture showed that the ratio of two isomers was about 1:1.

The procedure above constitutes a facile two-step method for the preparation of unsymmetrically 5,5'-disubstituted (*E*)-difuryl ethenes from easily obtainable furfuryl alcohol. The reaction can be run on a large scale without difficulty, and after the first step (reduction of furfuryl alcohol) no special purification of the reaction product is required. Both of the final substituents in the furan rings are quite reactive and make further syntheses possible.

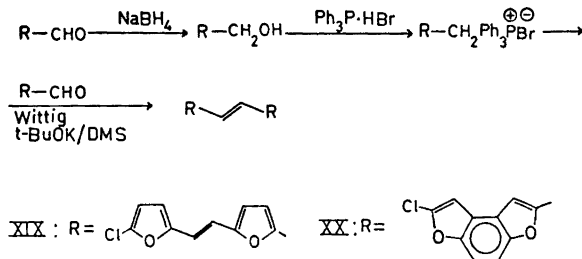
By the method of Kellog *et al.*² X was photocyclized in methanol to a 2,7-disubstituted benzo[1,2-b:4,3-b']difuran (XVIII) in a yield of 30 %.



Scheme 6.

With a longer reaction time in the photolysis the solvent, methanol, interacted with the formyl group giving the dimethylacetal of XVIII as a byproduct.

The preparation of furohelicenes from the derivatives of X and XVIII was also attempted (Scheme 7).



Scheme 7.

Both compounds XIX and XX were photolyzed under various conditions,³ but no furanoid products, such as the thienohelicenes prepared by Groen *et al.*,³ were formed. The linear tetrafuranoid compound (XIX) is quite labile (it decomposes slowly at room temperature) and therefore probably gave only insoluble (acetone), black resinous material. XX was relatively more stable under the conditions employed, because 75–85 % of the starting material was recovered unchanged after photolysis, and no reaction products, except tar, were formed.

EXPERIMENTAL

General. All melting points are uncorrected. The spectra were determined on the instruments described earlier.⁴ Furoin (I), thenoin (IV), and benzoin (V) were synthesized from the corresponding aldehydes by the method of Cardon and Lankelma.⁵ Vicinal diols IX, XI, and XIII were prepared by NaBH_4 reduction from I, IV, and V, respectively, the substituted vicinal diol XV from I *via* acetylation and NaBH_4 reduction, and XVI from I *via* the Grignard reaction. All diols were used without further purification.

Preparation of DMF complexes and reaction conditions. In the preparation of the DMF complexes in CH_2Cl_2 the procedure of Silverstein *et al.*⁶ was followed, and purified POCl_3 , SOCl_2 or COCl_2 (20 % in toluene) were employed. The equivalent amount or excess of the complexes were used in the reactions. Reaction times were from 15 min

to half an hour in dried, refluxing methylene chloride. Standard work-ups⁶ were employed.

Reaction products of the complexes

5-Chlorofurfuryl 2'-furyl ketone (II) and 5-formyl-2,2'-furyl (III). 4.20 g of I was used. Elution of the reaction mixture with CHCl_3 on a silica gel column gave 1.55 g (34 %) of II and 1.20 g (26 %) of III. Physical properties of II: m.p. 29–30°C (recryst. from petroleum ether b.p. 40–60°C); ν 1690, 880 cm^{-1} ; τ 2.42 (1 H d 1.5 Hz), 2.83 (1 H d 3.5 Hz), 3.50 (1 H dd 3.5 and 1.5 Hz), 3.75 (1 H d 3.5 Hz), 3.93 (1 H d 3.5 Hz), 5.91 (2 H s). (Found: C 57.14; H 3.33. Calc. for $\text{C}_{10}\text{H}_7\text{ClO}_3$: C 57.28; H 3.18.) Physical properties of III: m.p. 54–55°C (recryst. from petroleum ether b.p. 40–60°C); ν 3120, 1675, 870 cm^{-1} ; τ 0.55 (1 H s), 2.34 (1 H d 1.5 Hz), 3.15 (2 H d 3.5 Hz), 3.42 (1 H dd 3.5 and 1.5 Hz), 3.70 (1 H d 3.5 Hz). (Found: C 61.08; H 2.94. Calc. for $\text{C}_{11}\text{H}_6\text{O}_5$: C 60.55; H 2.75.) The yield of II after SOCl_2/DMF treatment of I was 54 % (traces of III were observed on a TLC plate) and after COCl_2/DMF treatment the yield of III was 47 % (only traces of II).

α -Chloro-2-thienyl 2'-thienyl ketone (VI). Yield 0.56 g (54 %), when 1.00 g of IV was used; viscous oil, very soon resinifying after a silica gel column treatment (CHCl_3); elemental analysis indicated chlorine; ν 3100, 2920, 1665, 1510, 1040, 710 cm^{-1} ; τ 2.10 (1 H m), 2.70 (5 H br. m), 3.55 (1 H s).

α -Chlorobenzyl phenyl ketone (VII). 1.00 g of V gave 0.95 g (96 %) of VII; m.p. 66–67°C (lit.⁷ m.p. 66–68°C); ν 3060, 1690 cm^{-1} ; τ 2.00 (2 H m), 2.60 (8 H m), 3.77 (1 H s).

(E)-1-(5-Chloro-2-furyl)-2-(5-formyl-2-furyl)ethene (X). 1.90 g of IX gave 1.10 g (52 %) of X; yellow needles from petroleum ether/ CHCl_3 ; m.p. 120°C; λ_{max} 273 (ϵ 8500), 366 (ϵ 34 600) nm; ν 1675, 1620 cm^{-1} ; τ 3.17 (1 H d 15.5 Hz), 2.98 (1 H d 15.5 Hz), 3.47 (1 H d 3.0 Hz), 2.72 (1 H d 3.0 Hz), 3.75 (1 H d 3.5 Hz), 3.53 (1 H d 3.5 Hz), 0.40 (1 H s); m/e 222 (100 %), 193 (12 %), 187 (5 %), 165 (25 %), 159 (71 %), 137 (17 %), 131 (22 %), 102 (34 %). (Found: C 59.71; H 3.27. Calc. for $\text{C}_{11}\text{H}_7\text{ClO}_3$: C 59.45; H 3.14.)

(E)-1(or 2)-(5-Chloro-2-furyl)-2(or 1)-(5-formyl-2-furyl)-1-butene (XVII). 1.00 g of XVI gave 0.97 g (47 %) of XVII, viscous pale yellow oil, which according to the NMR-spectrum was a 1:1 mixture of two isomers. τ 0.52 (1/2 H s), 0.55 (1/2 H s), 2.60–3.80 (5 H m), 7.25 (2 H q 7 Hz), 8.78 (3/2 H t 7 Hz), 8.80 (3/2 H t 7 Hz).

(E)-1-(5-Chloro-2-thienyl)-2-(2-thienyl)ethene (XII). 1.00 g of XI gave 0.35 g (35 %) of XII; yellow needles from $\text{EtOH}/\text{H}_2\text{O}$; m.p. 69–70°C; λ_{max} 258 (ϵ 7 900), 334 sh (ϵ 27 200), 346 (ϵ 29 000), 361 sh (ϵ 21 900) nm; ν 3050, 1560, 1520, 1435, 1040, 980, 930, 690 cm^{-1} ; τ 2.98 (1 H d 4 Hz), 3.08 (2 H m), 3.18 (2 H s), 3.30 (2 H s); m/e 226 (100 %), 191 (42 %), 190 (53 %), 181 (15 %), 158 (25 %), 147 (50 %). (Found: C 53.47; H 3.55. Calc. for $\text{C}_{10}\text{H}_6\text{ClS}_2$: C 53.10; H 3.10.)

1,2-Diphenylethanedioyl diformate (XIV). The yield was quantitative from XIII; white prisms from benzene/ CHCl_3 ; m.p. 167°C; ν 2930, 1705, 1150 cm^{-1} ; τ 1.95 (2 H s), 2.72 (10 H s), 3.74 (2 H s); m/e 242 (3 %), 224 (6 %), 197 (5 %), 179 (17 %), 165 (15 %), 152 (8 %), 135 (90 %), 105 (38 %), 77 (100 %). (Found: C 71.38; H 6.01. Calc. for $\text{C}_{16}\text{H}_{14}\text{O}_4$: C 71.11; H 5.81.)

Preparation of derivatives of X

7-Chlorobenzo[1,2-b:4,3-b']difuran-2-carboxaldehyde (XVIII). 0.500 g of X was dissolved in 500 ml of methanol and oxidizing agent⁸ (1.25 g of anh. CuCl_2 and 0.20 g of I_2) was added. The mixture was photolyzed with a Hanau TQ 81 UV-lamp under N_2 -atmosphere and tap water cooling for 8 h. Methanol was evaporated under reduced pressure, ether added and inorganic salts removed by washing with water. After drying and ether evaporation a yellow viscous oil was obtained, which after elution in a silica gel column with benzene gave 0.15 g (30 %) of white solid; m.p. 159–160°C (recryst. from petroleum ether/benzene); λ_{max} 265 sh (ϵ 5 900), 274 (ϵ 20 400), 285 (ϵ 23 600), 295 sh (ϵ 20 900) nm; ν 3110, 1680, 1520 cm^{-1} ; τ 0.10 (1 H s), 2.43 (2 H slight br. s), 2.62

(1 H s), 3.17 (1 H s); m/e 220 (100 %), 192 (9 %), 186 (9 %), 185 (6 %), 163 (19 %), 157 (38 %), 129 (34 %). (Found: C 59.85; H 2.18. Calc. for $C_{11}H_5ClO_3$: C 60.00; H 2.27.)

When the reaction time was extended to 24 h and excess of $CuCl_2/I_2$ was employed, the reaction of the solvent and the formyl group of XVIII occurred. 2.00 g of starting material (X) gave 0.25 g (13 %) of XVIII, 0.50 g (23 %) of dimethyl acetal of XVIII (XVIIIb), and 0.22 g of yellow material, which according to the NMR-spectrum was a mixture of (*E*)- and (*Z*)-forms of X. The diluted hydrochloric acid treatment of XVIIIb produced a quantitative yield of XVIII. XVIIIb: viscous pale yellow oil; λ_{max} 266 sh (ϵ 9000), 273 (ϵ 20 100), 284 (ϵ 28 000), 294 sh (ϵ 6100) nm; τ 2.56 (2 H s), 2.98 (1 H s), 3.25 (1 H s), 4.32 (1 H s), 6.56 (6 H s).

(*E*)-1,2-Di[5-(*E*)-2-(5-chloro-2-furyl)-1-ethenyl]-2-furyl] ethene (XIX). The Wittig compound XXI was prepared from PhP.HBr⁸ and $NaBH_4$ reduced X by the procedure of Saikachi *et al.*⁹ The Wittig reaction was accomplished in DMS with *t*-BuOK.¹⁰ 1.00 g of XXI and 0.70 g of X gave after column chromatography with benzene and recrystallization from benzene/petroleum ether 0.60 g (46 %) of dark red needles; m.p. 182°C (d); λ_{max} 282 sh (ϵ 11 700), 286 (ϵ 12 400), 330 (ϵ 9000), 345 (ϵ 13 700), 416 sh (ϵ 16 500), 440 (ϵ 24 700), 470 (ϵ 21 300) nm; ν 1510, 1460, 970, 955, 940 cm^{-1} ; τ 3.15 (6 H m), 3.65 (8 H m); m/e 412 (100 %), 377 (8 %), 349 (21 %), 321 (5 %), 313 (6 %), 285 (6 %), 257 (8 %), 229 (7 %), 207 (22 %), 206 (30 %), 165 (14 %), 143 (20 %). (Found: C 75.66; H 3.89. Calc. for $C_{22}H_{14}Cl_2$: C 75.86; H 4.02.)

(*E*)-1,2-Di(7-chloro-2-benzo[1,2-*b*:4,3-*b'*]difuran)ethene (XX). The preparation of the phosphorus compound XXI from XVIII and the Wittig reaction with XXI and XVIII were performed as above. After a column chromatography with benzene and recrystallization from cyclohexane/benzene 0.50 g of XXI and 0.20 g of XVIII gave 0.25 g (62 %) orange needles. The compound (XX) had a strong, blue fluorescence in benzene solution. XX: m.p. 264°C; λ_{max} 347 sh (ϵ 28 500), 363 (ϵ 55 200), 383 (ϵ 9600), 407 (ϵ 97 900) nm; ν 3120, 1525, 970, 950 cm^{-1} ; m/e 408 (100 %), 376 (17 %), 374 (52 %), 345 (20 %), 276 (43 %), 204 (20 %).

Photolysis of XIX and XX. Both XIX and XX were photolyzed under various conditions³ and with various oxidizing agents.² In every case XIX produced only resinous material. XX gave no reaction products, and 75–85 % of the starting material was recovered after photolysis (identification with TLC and UV-spectroscopy).

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