

MONOFUNCTIONALIZATION STUDY OF FURAN-2,5-DICARBOXALDEHYDE. CONFORMATIONAL ANALYSIS AND MODEL REACTIONS

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Abstract- The possible monofunctionalization of furan-2,5-dicarboxaldehyde is verified by means of several model reactions. On the other hand conformational analysis of FDC is analyzed by a combined experimental dipole moment determination-theoretical MNDO calculation.

Furan-2,5-dicarboxaldehyde, FDC, is an important synthetic intermediate isolated from the biomass¹ and useful for the preparation of a variety of compounds of industrial and pharmacological interest². It is also a widely used starting material both in bridged annulene and crown ether chemistry³. Largely, the reactions of FDC imply the functionalization of both formyl groups^{4,5}. Thus, direct monofunctionalization of FDC appears to be desirable in order to improve the synthetic versatility of this compound.

Direct functionalization of one carbonyl group in FDC has been performed for the following reactions: i) reaction of 1 with MeOH/TsOH afforded the monoacetal 5¹²; ii) reaction with acetone yielded 6¹³; iii) other aldolic condensations with

aromatic ketones gave products 7 and 8 depending on the reaction conditions (Table 1)

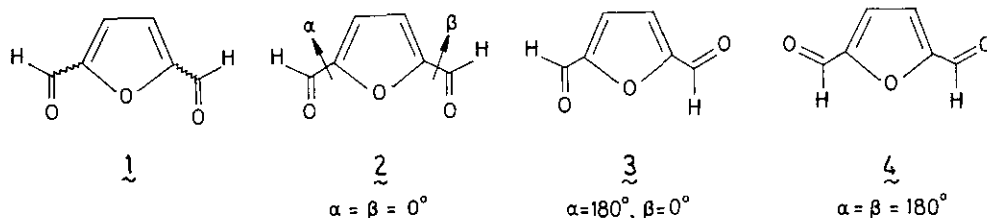


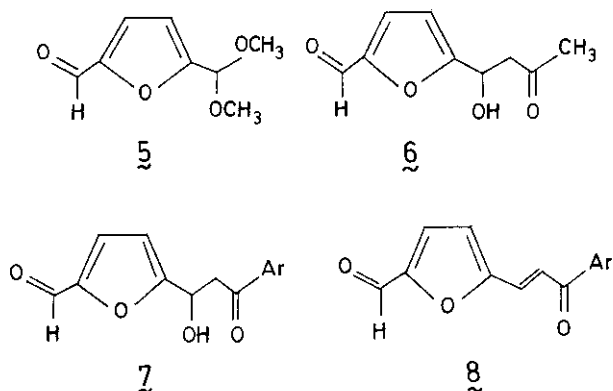
Table 1

Aldolic condensations of FDC with aromatic ketones

Ar-	Base	Solvent	Conditions		Yield(%) ^a	
			FDC/RCOAr	time	<u>7</u>	<u>8</u>
Phenyl	NaOH, 10%	EtOH	1:1	40 min	14	73
2-Thienyl	NaOH, 10%	EtOH	1:1	40 min	16	42
p-Methoxyphenyl	NaOH, 10%	EtOH	1:1	40 min	25	--
p-Nitrophenyl	NaOH, 10%	EtOH	1:1	40 min	--	--
2-Furyl	NaOH, 10%	EtOH	1:1	40 min	30	36
p-Methoxyphenyl	NaOH, 1%	EtOH/H ₂ O	1:1	2 days	10	--
p-Methoxyphenyl	NaOH, 1%	EtOH/H ₂ O	1:1.5	7 days	12	--
p-Methoxyphenyl	NaOH, 1%	EtOH/H ₂ O	1:2	3 days	18	--
p-Methoxyphenyl	NaOH, 1%	EtOH/H ₂ O	1:4	2 days	60	--
Phenyl	NaOH, 1%	EtOH/H ₂ O	1:1	4 days	41	49
2-Furyl	NaOH, 1%	EtOH/H ₂ O	1:1	2 days	--	--
2-Thienyl	NaOH, 1%	EtOH/H ₂ O	1:1	4 days	32	30
p-Nitrophenyl	NaOH, 1%	EtOH/H ₂ O	1:1	1 day	17	43

a) In pure, isolated product. See reference 14.

On the other hand, the conformational equivalence of both formyl groups has been evaluated in the following way: For 1 there are three a priori more stable conformations with both formyl groups coplanar with the furan ring: 2, ZZ; 3, EZ, and 4, EE.



SCF-MNDO⁶ calculations show populations of 7.1% for 2, 62% for 3 and 30.9% for 4 obtained from the theoretical heats of formation of the three coplanar⁷ conformations. The calculated dipole moment is $\mu = 2.57$ D. The experimental dipole moment⁸ ($\mu = 3.16$ D in benzene and in cyclohexane) is in reasonably good agreement with the theoretical one⁹. This indicates that in FDC there is a conformational equilibrium where the EZ conformation 3 has the biggest contribution^{10,11}.

In conclusion, conformational analysis of FDC indicates no equivalence of both aldehyde groups. Experimental comprobation has been performed for two model reactions: monoprotection with MeOH/TsOH and aldolic condensations. Other reactions and synthetic utility of monofunctionalized FDC are being currently explored in our laboratories.

ACKNOWLEDGEMENTS

This research was in part sponsored by the CICYT (Ministerio de Educación y Ciencia, Spain). Grants No. 320/84 and 2953/83. Two of us (C.D. and A.G.C.) thank the Comunidad Autónoma de Madrid (Consejería de Educación) for a grant.

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stimated in, at least, 2.75 Kcal/mol.

8. Determined in benzene and in cyclohexane solutions at concentrations between $1 \cdot 10^{-3} < w_2 < 5.5 \cdot 10^{-3}$ for benzene solutions and $2 \cdot 10^{-4} < w_2 < 9 \cdot 10^{-4}$ for cyclohexane ones, expressed as solute weight fraction, using the Debye method, by application of Halverstadt and Kumler and Guggenheim-Smith equations. Full experimental details including molar polarization and molar refraction of solute at infinite dilution, and dependences of dielectric constants (ϵ), refractive index (n), and dependence of specific volume (v) with concentrations ranging will be published elsewhere and be done upon request. Correspondence to Prof. I.Hernández-Fuentes. For the method applied, see P.Debye, Phys.Z., 1912, 13, 97; J.F.Halverstadt and D.W.Kumler, J.Am.Chem.Soc., 1942, 64, 2988; E.Guggenheim, Trans.Faraday Soc., 1949, 95, 714; ibid., 1951, 47, 573; J.W.Smith, Ibid., 1950, 46, 394
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12. From 124 mg FDC (1 mmol) in anhydrous methanol (15 ml) with a trace amount of p-toluenesulphonic acid at reflux during 18 h. Yield 73%. Ir (CCl₄) 2829, 1680, 1580, 1520 cm⁻¹. ¹H-Nmr (60 MHz, CDCl₃) 3.4 (s, 6H, OMe); 5.4 (s, 1H, CH); 7.1,

6.6 (AB_q, 2H, J=4Hz, H_{furan}); 9.56 (s, 1H, Aldehyde).

13. From 248 mg FDC (2 mmol) in 10 ml of a mixture EtOH:H₂O (1:1), 1.17 g of acetone (20 mmol) and eight drops of 1% NaOH, at 0°C. Reaction time, 1h. Yield 65%, bp 200°C (0.1 mmHg). Ir (CCl₄) 3400, 2840, 2920, 1670, 1710 cm⁻¹. ¹H-Nmr (60 MHz, CDCl₃) 2.23 (s, 3H, H-C(9)); 3.0 (d, 2H, J=6Hz, H-C(7)); 4.0 (s, broad, 1H, OH); 5.2 (t, 1H, J=6Hz, H-C(6)); 6.5 (d, 1H, J=4Hz, H-C(4)); 7.2 (d, 1H, J=4 Hz, H-C(3)); 9.5 (s, 1H, H-C(1)). ¹³C-Nmr (80 MHz, CDCl₃) 207 (C(8)); 177 (C(1)); 162 (C(2)); 152 (C(5)); 123 (C(3)); 109 (C(4)); 63 (C(6)); 48 (C(7)); 30 (C(9)).

Reaction of FDC with acetone did not afford the expected aldol. In the presence of a reducing medium (H₂-BaSO₄) the reduced product may be isolated. See ref 2c and:

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14. All reactions were performed at 0°C. Products 7 and 8 have been separated by silica gel column chromatography employing a mixture of n-hexane/ethyl acetate (1:2). Spectroscopic and analytical data are in good agreement with the proposed structures. Full details will be published elsewhere and may be done upon request. Correspondence to Prof.J.Plumet.

Received, 8th December, 1988