

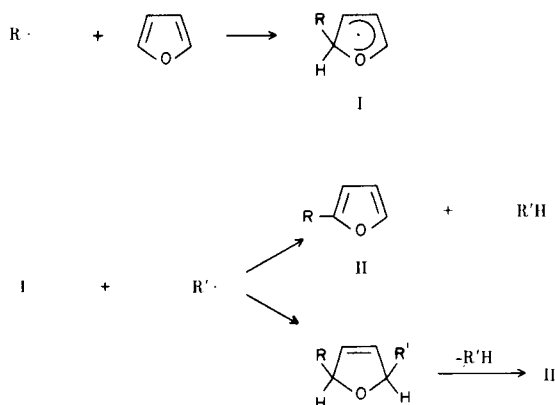
## The Arylation of Furan

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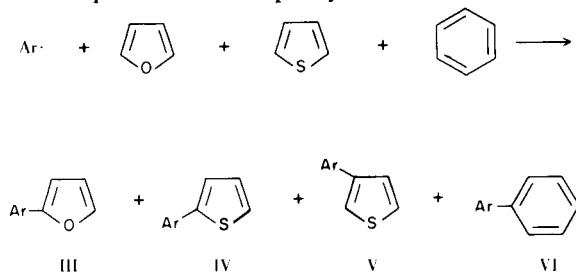
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Several reactions between furan and radical precursors are reported in the literature, and it appears that this five membered heterocycle can undergo two types of reaction, addition or substitution, depending on the reagent employed.



Addition compounds are the main products of the reaction between furan and two common phenyl radical precursors, dibenzoyl peroxyde (1) and phenylazotriphenylmethane (2,3); substitution, however, becomes the predominant reaction when furan is allowed to interact with other phenylating agents. Thus from the decomposition of the *N*-nitrosoacetanilide, from the aprotic diazotization of aniline and from the Gomberg-Hey reaction, 2-phenylfuran was the only reaction product (2). Competitive experiments between furan and benzene and between furan and thiophene have been carried out in order to determine the reactivity of furan relative to benzene ( $\frac{F}{B}K$ ) and thiophene ( $\frac{F}{T}K$ ) in respect to several *meta* and *para*-substituted phenyl radicals.



The experimental procedure employed was described previously (4). The relative reactivities  $\frac{F}{B}K$ ,  $\frac{F}{T}K$  and  $\frac{F}{B}k_2$  were determined from the quantities of biaryls, arylfurans and arylthiophenes determined in the analysis using the relationships:

$$(1) \quad \frac{F}{B}K = \frac{\text{moles [III]}}{\text{moles [VI]}}$$

$$(2) \quad \frac{F}{T}K = \frac{\text{moles [III]}}{\text{moles [IV] + [V]}}$$

$$(3) \quad \frac{F}{B}k_2 = \frac{F}{B}K \times 3$$

Relationship 3 holds because furan is phenylated only in position 2.

Table I summarizes the results of the reaction of furan with the unsubstituted phenyl radical generated from the decomposition of *N*-nitrosoacetanilide and from the aprotic diazotization of aniline with amyl nitrite. In the latter cases, the reactivity of furan relative to benzene and

TABLE I  
Relative Reactivities of Phenylation of  
Furan ( $\frac{F}{B}K$ ) and Thiophene ( $\frac{T}{B}K$ )

Phenylating Agent	$\frac{F}{B}K$	Relative Reactivities		
		$\frac{F}{T}K$	Calc.	Exp.
PhNH <sub>2</sub> + AmONO (c)	11.5	4.4	2.6	2.6 (b)
PhNH <sub>2</sub> + AmONO (d)	11.8	4.45		2.65
PhNH <sub>2</sub> + AmONO (e)	11.3	4.6		2.45
PhN(NO)COCH <sub>3</sub> (c)	12.4	4.6	2.7	2.6
Average	11.7	4.5		2.6

(a) The values have been obtained from the relationship  $\frac{T}{B}K = \frac{T}{F}K \cdot \frac{F}{B}K$ . (b) Cfr. ref. 4. (c) Equimolecular mixtures of the two solvents under investigation have been employed. (d) Furan, benzene, and thiophene were employed together in the ratio of 1:1:1. (e) The ratio of furan, benzene, and thiophene was 1:10:5; the statistical correction was then applied to the experimental values.

TABLE II (a)

Reactivities of Furan Relative to Benzene ( $\frac{F}{B}K$ ) and Thiophene ( $\frac{T}{B}K$ ) Towards *meta* and *para* Substituted Phenyl Radicals, Relative Reactivities of Thiophene ( $\frac{T}{B}K$ ), and Partial Rate Factors for the Arylation of Furan ( $\frac{F}{B}k_2$ ).

Radical	$\frac{F}{B}K$	$\frac{F}{B}k_2$	$\frac{F}{T}K$	$\frac{T}{B}K$ (b)	$\frac{T}{B}K$ (c)
<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	6.8	20.4	4.15	1.7	1.65
<i>p</i> -McC <sub>6</sub> H <sub>4</sub>	11.4	34.2	4.7	2.4	2.44
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	14.9	44.7	4.95	2.9	3.0
<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	28.1	84.3	7.75	3.6	3.63
<i>m</i> -McC <sub>6</sub> H <sub>4</sub>	11.7	35.1	4.55	2.4	2.57
<i>m</i> -ClC <sub>6</sub> H <sub>4</sub>	18.4	55.2	5.0	3.13	3.7
C <sub>6</sub> H <sub>5</sub>	11.7	35.1	4.5	2.6	2.6

(a) The values of the relative reactivities have been obtained by averaging the results obtained from experiments carried out with equimolecular mixtures of two solvents with those in which the three aromatic compounds were employed together. (b) Taken from ref. 4. (c) The figures have been obtained from the relationship  $\frac{T}{B}K = \frac{F}{B}K / \frac{F}{T}K$ .

thiophene was also determined from experiments in which the three substrates were allowed to compete together for the phenyl radical; the three compounds furan, benzene, and thiophene, were used in an equimolecular mixture and in the ratio of 1:10:5. These experiments permitted the determination of all the relative reactivities,  $\frac{F}{B}K$ ,  $\frac{F}{T}K$  and  $\frac{T}{B}K$ , from a single experiment. Moreover, from the competitive experiments of furan and benzene and furan and thiophene, the reactivity of thiophene towards benzene can be calculated according to the relationship,  $\frac{T}{B}K = \frac{F}{B}K / \frac{F}{T}K$ , which has been found to be applicable in homolytic aromatic substitutions (5). The values obtained are compared in Table I with those previously determined (4) from direct experiments between thiophene and benzene. Examination of the data collected in Table I shows that good agreement is obtained from all these experiments, indicating that no particular effect is involved in the phenylations investigated and that the reaction proceeds without evidence of preferential solvation by one of the solvents. In every case, the substitution in furan took place only in position 2 while thiophene was phenylated both in the 2 and 3-positions in the ratio of 93:7.

Due to the higher reactivity of furan with respect to benzene in electrophilic substitution, it can be predicted that the presence in the phenyl radical of electron withdrawing substituents, which renders the radical electrophilic, will increase the relative reactivity  $\frac{F}{B}K$ ; on the contrary, with nucleophilic aryl radicals, the  $\frac{F}{B}K$  is expected to decrease. This has been recently found to occur

in the homolytic arylation of thiophene (4) and should also be encountered, to a greater extent, in furan. Experiments were carried out in which aryl radicals, generated from the aprotic diazotization of substituted anilines, were allowed to react with equimolecular mixtures of furan and benzene, furan and thiophene, and furan, benzene and thiophene. Only substitution in the 2-position was observed in the case of furan with all the aryl radicals employed. Table II summarizes the averaged results of these experiments, as well as the values of the partial rate factors ( $\frac{F}{B}k_2$ ) for the 2-position of furan.

The presence of substituents on the attacking radical markedly influences the values of the relative reactivities of furan in respect to benzene, in the sense that electron-withdrawing groups lead to an increase and electron-releasing to a decrease of  $\frac{F}{B}K$  in agreement with expectation.

Moreover, the log of partial rate factors for the arylation of furan ( $\frac{F}{B}k_2$ ) can be linearly correlated with the  $\sigma^+$  values of the substituents present in the attacking radicals. The resulting straight line has a slope of +0.46 (correlation coefficient 0.970), confirming the known activation of the 2-position of furan towards electrophilic attack. A similar correlation was also found in the case of thiophene and the slope has the value of +0.225 (correlation coefficient 0.977) (4).

From the results accumulated from the study of *meta*- and *para*-substituted phenyl radicals it can thus be concluded that the arylation of furan and thiophene follow an identical path; a comparison of the relative reactivities of the two heterocycles indicated, moreover, that furan possesses a susceptibility towards polarized radicals greater than that observed for thiophene.

#### EXPERIMENTAL

Gas-chromatographic analyses were carried out with a Varian 1520 gas-chromatograph equipped with flame-ionization and gas density balance detectors. Furan, thiophene, and benzene were commercial products of the highest purity grade available, and were carefully distilled before the reaction.

#### Reference Compounds.

Substituted biaryls and phenyl thiophenes were prepared according to the methods reported in a previous work (4). 2- and 3-Phenylfuran (6,7), 2-*para*-tolylfuran (6), 2-*para*-methoxyphenylfuran (6), 2-*para*- and *meta*-chlorophenylfuran (6) and 2-*para*-nitrophenylfuran (8) were prepared as reported in the literature. 2-*meta*-Tolylfuran.

This compound (oil, Kp 130°/3 mm) was separated and identified directly from an arylation reaction.

*Anal.* Calcd. for C<sub>11</sub>H<sub>10</sub>O: C, 83.54; H, 6.33. Found: C, 82.63; H, 6.47.

#### Arylation Procedure.

Competitive experiments were carried out by the procedure

described previously (4,2). The yields in phenylation products were 40-70%.

Gas chromatographic analysis was performed in all the cases examined with a 10% FFAP on Aeropak 30 (80-100 mesh) column (2 mt x 1/8"), with the exception of the reaction mixtures relative to the *p*-methoxyphenylation of furan/benzene, furan/thiophene and furan/benzene/thiophene. In these cases, better results were obtained with a 5% LAC 728 on Aeropak 30 (80-100) column (2 mt x 1/8").

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