Substituent Effects in the Trifluoroacetylation of Substituted Thiophens, Furans, and Pyrroles

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Summary Furan, thiophen, and pyrrole show considerable differences in sensitivity to substituent effects in electrophilic substitution.

ELECTROPHILIC substitutions at the thiophen ring exhibit a selectivity which is always somewhat lower than that of the corresponding reactions at the benzene ring. Thus, the values of the ρ constants for bromination,[1] chlorination,[2] protodetritiation,[3] and acetylation[4] of 2-substituted thiophens are somewhat smaller than the ρ values for the corresponding substitutions of benzene derivatives.

These differences in ρ values have been ascribed to the occurrence of "earlier" transition states in substitution of thiophens.[3]

We are now able to report data which permit a comparison of the "selectivities" of the same electrophilic substitution (trifluoroacetylation by trifluoroacetic anhydride) in the three fundamental five-membered rings: furan, thiophen, and pyrrole.

The relative rates of trifluoroacetylation of a number of 2-substituted thiophens, furans, and pyrroles in dichloroethane at 75° have been determined by using a competitive procedure.[6] The relevant values are assembled in the Table.

The log k/k_H for thiophens and furans correlate very well with σ_p^+ constants, yielding ρ values of $-7{\cdot}4$ and $-10{\cdot}3$, respectively.

The available data for pyrroles are limited to the alkyl derivatives and do not permit the testing of the applicability of a linear free-energy relationship; nevertheless, they do show that the sensitivity of the pyrrole ring to substituent effects is much smaller than that of the other two rings. The observed low "selectivity" of the pyrrole ring is in keeping with the Hammond postulate,[7] according to which the transition state of the substitution will lie further from the Wheland intermediate because of the very high reactivity of this ring.[6,8]

Relative rates of trifluoroacetylation of 2-substituted furans, thiophens and pyrroles in dichloroethane at 75°

		k/k_0[a]	
Substituent	Furans	Thiophens	Pyrroles
OCH_3	—	$1{\cdot}8 \times 10^{6}$[b]	—
SCH_3	—	$5{\cdot}2 \times 10^{3}$[b]	—
CH_3	$1{\cdot}7 \times 10^{3}$[b]	$3{\cdot}8 \times 10^{2}$[b]	23·8
C_2H_5	$1{\cdot}4 \times 10^{3}$	$5{\cdot}2 \times 10^{2}$	24·8
$C_4H_9{}^t$	—	$5{\cdot}4 \times 10^{2}$	24·8
C_6H_5	—	$1{\cdot}1 \times 10^{2}$	—
H	1	1	1
Cl	—	$5{\cdot}8 \times 10^{-1}$	—
Br	9×10^{-3}	$4{\cdot}6 \times 10^{-1}$	—

[a] Relative rates of substitution at position 5. The values are corrected for the statistical factor.

[b] Calculated from data of ref. 6.

The results for furan are rather surprising. Furan is, in fact, intermediate in reactivity between thiophen and pyrrole[6,8] and, therefore, an intermediate "selectivity" would be expected. In contrast with these predictions, the ρ value for the trifluoroacetylation of furans is more negative than that for thiophens.

Although other data on other electrophilic substitutions would be desirable before generalising this observation, it may be interesting to note that the same trend (*i.e.*, a sensitivity of the furan ring to substituent effects greater even than that of benzene) has been observed in two other reactions, which can be considered, under certain aspects, similar to the electrophilic substitutions: the molecular ionization in gas phase[9] and the solvolysis of 1-arylethyl *p*-nitrobenzoates.[10]

We cannot find convincing explanations for this anomaly, but it is possible that it is connected with the greater "bond fixation" in the furan ring.

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