

## Relative Reactivities of Thiophen, Furan, and Pyrrole Rings in Electrophilic Substitutions: Bromination of the 2-Methoxycarbonyl Derivatives

By P. LINDA and G. MARINO\*

(Istituto Chimico, Università di Trieste, Italy)

IN the preceding Communication<sup>1</sup> the relative reactivities of the five-membered heterocyclic rings towards trifluoroacetylation have been reported. In order to confirm the general validity of those results, an extension to other electrophilic substitutions was desirable.

We now give a preliminary account of a kinetic study on the bromination by molecular bromine of the 2-methoxycarbonyl derivatives of furan, thiophen, and pyrrole.

Under the conditions chosen for the kinetic study, *i.e.*, in acetic acid solution and in the dark, all the substrates examined give the monobromo-substituted products in high yield. The isomer distribution, as determined by v.p.c. analysis of the reaction products, was the following: 100% 5-bromo-isomer for furan and thiophen derivatives, 23% 5-bromo- and 77% 4-bromo-isomer for the pyrrole derivative.

No side-reactions, such as addition to the double bonds, polymerisation, or ring cleavage were observed.

Due to the very large reactivity range, it was not possible to carry out all the kinetic measurements in the same solvent. Accordingly, we used 50% aqueous acetic acid as solvent for the less reactive thiophen and furan derivatives and 100% acetic

acid for the more reactive 2-methoxycarbonyl-pyrrole. A compound exhibiting intermediate reactivity, unsubstituted thiophen, was examined in both solvents. It has been assumed by many authors in similar studies<sup>2</sup> that the relative rates are not significantly affected by such differences in solvent composition.

The kinetics of bromination of these heterocyclic derivatives show exactly the same characteristics as the bromination of benzene derivatives.<sup>3</sup> The reaction is first order in bromine and in substrate when it is carried out in the presence of a large excess of lithium bromide.

Experiments were made at several initial Br<sup>-</sup> concentrations, maintaining the ionic strength constant at 0.2M by adding appropriate amounts of lithium perchlorate.

The specific rate-constants for the reaction with free molecular bromine, were determined according to the procedure recommended by Bell and Rawlinson<sup>4</sup> from the plots of  $k_{\text{obs}}(1 + K[\text{Br}^-])$  against  $[\text{Br}^-]$ . ( $K$  is the equilibrium constant for  $\text{Br}_2 + \text{Br}^- \rightleftharpoons \text{Br}_3^-$ ). Such plots were linear in all cases. The second-order rate constants were extrapolated to zero bromide ion concentration and the relative rates of bromination at the  $\alpha$ -position are reported in the Table.

TABLE

*Kinetic data for the bromination of some derivatives of furan, thiophen, and pyrrole*

Substrate	Solvent	$k^a$	$k/k^{0b}$
2-Methoxycarbonylthiophen .. ..	50% AcOH	$1.6 \times 10^{-3}$	1
2-Methoxycarbonylfuran .. ..	"	$1.9 \times 10^{-1}$	$1.2 \times 10^2$
Thiophen .. ..	"	$3.6 \times 10^3$	
" .. ..	100% "	$6.2 \times 10^{-1}$	
2-Methoxycarbonylpyrrole .. ..	"	$6.6 \times 10^2$	$5.5 \times 10^3$

<sup>a</sup> Second-order rate constants for bromination by free molecular bromine, in l. moles<sup>-1</sup> sec.<sup>-1</sup> at 25°.

<sup>b</sup> Relative rates for bromination at the  $\alpha$ -position.

The relative rates of bromination parallel those of trifluoroacetylation.<sup>1</sup> In this case also, the reactivity order of these rings is thiophen < furan < pyrrole, the largest jump in reactivity being between the last two mentioned.

The agreement between trifluoroacetylation and bromination data represents a mutual confirmation of the applicability of the diverse experimental approaches used in the two reactions.

Since the reactivity of thiophen relative to

benzene had been determined in a previous study,<sup>5</sup> we are now able to calculate the partial rate factors (with respect to a single position of benzene) for the  $\alpha$ -positions of the three five-membered rings: thiophen  $5.1 \times 10^9$ , furan  $6.1 \times 10^{11}$ , and pyrrole  $2.8 \times 10^{18}$ .

Full experimental details and a more complete discussion on the subject will be reported elsewhere.

(Received, April 17th, 1967; Com. 371.)

<sup>1</sup> S. Clementi, F. Genel, and G. Marino, *Chem. Comm.*, 1967, 498.

<sup>2</sup> (a) Un-Jin, P. Zimmerman, and E. Berliner, *J. Amer. Chem. Soc.*, 1962, **84**, 3953; (b) H. C. Brown and L. M. Stock, *ibid.*, 1957, **79**, 1421.

<sup>3</sup> (a) E. Berliner and M. C. Beckett, *J. Amer. Chem. Soc.*, 1957, **79**, 1425; (b) P. B. D. de la Mare, O. M. H. el Dusouqui, J. T. Tillet, and M. Zeltner, *J. Chem. Soc.*, 1964, 5306; (c) E. Berliner and J. C. Powers, *J. Amer. Chem. Soc.*, 1961, **83**, 905.

<sup>4</sup> R. P. Bell and D. J. Rawlinson, *J. Chem. Soc.*, 1961, 63.

<sup>5</sup> G. Marino, *Tetrahedron*, 1965, **21**, 843.