Kinetics of the Reaction of Some 3- and 5-Substituted 2-Thenoyl and *ortho*- and *para*-Benzoyl Chlorides with Aniline in Benzene

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The rate of the reaction of some 3-substituted 2-thenoyl chlorides with aniline is measured in benzene at different temperatures, in comparison with the corresponding *ortho*-substituted benzoyl chlorides. For comparison are also reported the rate constants for 5-substituted 2-thenoyl chlorides and *para*-substituted benzoyl chlorides. Thienyl compounds react slower than phenyl derivatives. The 3-substituted 2-thenoyl and *ortho*-substituted benzoyl chloride reactions are faster than those of the corresponding 5- and *para*-derivatives.

RECENTLY we have studied the kinetics of the reaction of 2-[1] and 3-thenoyl [2,3] and 2- and 3-furoyl chlorides [2,4] with substituted anilines, 2- and 3-chloroacetylfurans and 2- and 3-chloroacetylthiophens with triethyl phosphite,[5] and basic [6] and acid hydrolysis [7] of 2- and 3-furanilides and 2- and 3-thenanilides for the purpose of comparing the reactivity of thiophen and furan rings with that of the benzene nucleus. The data indicate that the heterocyclic rings, depending on the pattern of substitution and the reaction considered, may act as electron donors or acceptors.

Spinelli *et al.* have found examples of linear free energy *ortho*-correlations for some thiophen derivatives in reactions which are not satisfactorily correlated in the benzene series.[8-11] This difference in behaviour is probably linked to the geometry of the thiophen ring.

TABLE 1

Second-order rate constants and activation parameters for the reaction of substituted 2-thenoyl and benzoyl chlorides with aniline

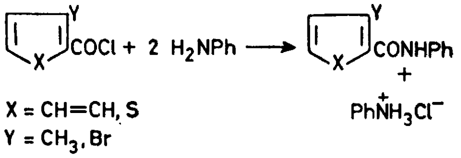
2-Thenoyl substituent	10^2k/l mol^{-1} s^{-1} [a] 15 °C	25 °C	40 °C	log *A*	E_a [b]/kcal mol^{-1}	ΔS^* [c]/cal mol^{-1} K^{-1}
H [d]		2.52		4.25	7.94	−41.1
3-CH_3 [e]	1.23	1.99	3.82	4.25	8.12	−41.1
5-CH_3 [f]		1.02		4.29	8.56	−40.9
3-Br [e]	9.46	14.3	24.9	4.24	6.93	−41.1
5-Br [e]	4.31	6.24	11.8	4.14	7.26	−41.6
Benzoyl substituent						
H [e,g]	3.94	6.16	10.8	4.07	7.21	−41.9
o-CH_3 [e]	2.85	4.45	8.20	4.20	7.58	−41.3
p-CH_3 [e,h]	2.45	3.87	7.20	4.25	7.72	−41.1
o-Br [e]	12.8	18.7	33.2	4.30	6.85	−40.8
p-Br [e,i]	7.97	12.0	21.6	4.33	7.16	−40.7

[a] Rate constants are accurate to ±3%. [b] The estimated precision is *ca.* ±0.7 kcal mol^{-1}. [c] At 25 °C, the estimated precision is *ca.* ±3 cal mol^{-1} K^{-1}. [d] See ref. 1. [e] This work. [f] See ref. 13. [g] E. Tommila and T. Vihavainen, *Acta Chem. Scand.*, 1968, **22**, 3224. [h] E. G. Williams and C. N. Hinshelwood, *J. Chem. Soc.*, 1934, 1079. [i] See ref. 14.

We report here a kinetic study of the reaction of some 3-substituted 2-thenoyl chlorides and the corresponding *ortho*-substituted benzoyl chlorides with aniline in benzene with the aim of studying the effect of the substituents on the rate.

RESULTS AND DISCUSSION

The reaction of acid chlorides with aniline takes place quantitatively according to the stoicheiometric equation (1). For comparison purposes the rate constants of the corresponding *para*-substituted benzoyl chlorides were also measured. The reactions were followed kinetically as previously described [2,3] and in all cases the compounds gave excellent second-order kinetics. Second-order rate constants are reported in Table 1 together with those



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for the corresponding 5-substituted 2-thenoyl chlorides and *para*-substituted benzoyl chlorides. The rate constants of the reaction of the thenoyl chlorides are slower than those of the benzoyl chlorides, as found previously.[1,3]

The results show that the methyl group retards and the bromine substituent accelerates the reaction. The reactivity of 3- and *ortho*-derivatives is greater than that of 5- and *para*-analogues. For the methyl derivatives this can be ascribed to the weaker conjugation of the negative charge inducted by the methyl group at the reaction centre. For the bromo-derivatives the inductive effect of the bromine atom in the 3- and *ortho*-positions is greater than that in the 5- and *para*-positions, as noted in the reaction of *o*- and *p*-chlorobenzoyl chlorides with aniline.[12]

The activation parameters (Table 1) show a regular variation with the substituent in the acid chloride, the effect of the substituent being to modify the activation energy while log *A* remains approximately constant, as found previously [3,4] and in the *o*-chloro- and 2,6-dichlorobenzoyl chloride reactions.[12] The large negative entropies of activation are similar to those found for 2- [1] and 3-thenoyl [3] and 2- and 3-furoyl chloride reactions.[2,4]

We found that 2-thenoyl chloride reacts more slowly than benzoyl chloride although 2-thenoic acid is stronger than benzoic acid.[1] The data in Tables 2 and 3 also indicate that 3- and 5-substituted 2-thenoyl chlorides, compared with the corresponding *ortho*- and *para*-substituted benzoyl chlorides, react more slowly than expected from the pK_a values of thenoic acids. The slower reaction rate of thenoyl chlorides, in comparison with that of benzoyl chlorides, was ascribed to resonance between the thiophen ring and the carbonyl group which stabilizes it and makes it less reactive towards aniline, than the carbonyl group of benzoyl chloride.[1]

TABLE 2

I.r. carbonyl frequencies of 3- and 5-substituted 2-thenoyl chlorides in CCl_4, log *k* at 25° for the reaction with aniline, and pK_a of the corresponding acids

Substituent	$\nu_{C=O}$/cm^{-1}	log *k*	pK_a [a]
H	1 753 [b]	−1.5986 [d]	3.51
3-CH_3	1 752 [c]	−1.7011 [c]	3.90
5-CH_3	1 750 [b]	−1.9914 [c]	3.74
5-CH_3O	1 742 [c]	−2.3170 [e]	3.78
5-Cl	1 750 [b]	−1.2299 [e]	3.30
3-Br	1 761 [c]	−0.8447 [c]	3.24
5-Br	1 750 [b]	−1.2048 [c]	3.27
5-NO_2	1 767 [b]	−0.3737 [e]	2.78

[a] In water at 25°, see ref. 10. [b] A. Arcoria, S. Fisichella, and D. Sciotto, *Tetrahedron Letters*, 1973, 2907. [c] This work. [d] See ref. 1. [e] See ref. 13.

TABLE 3

I.r. carbonyl frequencies of substituted benzoyl chlorides in CCl_4, log *k* at 25° for the reaction with aniline, and pK_a of the corresponding acids

Substituent	$\nu_{C=O}$/cm^{-1} [a]	log *k*	pK_a [b]
H	1 782	−1.2104 [c]	4.17
o-CH_3	1 781	−1.3516 [c]	3.91
m-CH_3	1 767	−1.3372 [d]	4.27
p-CH_3	1 777	−1.4112 [c]	4.37
p-CH_3O	1 777	−1.8268 [d]	4.47
o-Cl	1 796	−0.5171 [e]	2.94
m-Cl	1 818	−0.7055 [e]	3.83
p-Cl	1 783	−0.9706 [e]	3.98
o-Br	1 795	−0.7282 [c]	2.85
m-Br	1 804	−0.7825 [d]	3.81
p-Br	1 779	−0.9208 [c]	3.97
m-I	1 797	−0.8125 [d]	3.85
p-NO_2	1 793	−0.2358 [f]	3.43

[a] See ref. 18. [b] In water at 25°, A. Albert, E. P. Serjeant, 'Ionization Constants of Acids and Bases,' Methuen, London, Wiley, New York, 1962, p. 127. [c] This work. [d] See ref. 14. [e] See ref. 12. [f] E. G. Williams and C. N. Hinshelwood, *J. Chem. Soc.*, 1934, 1079.

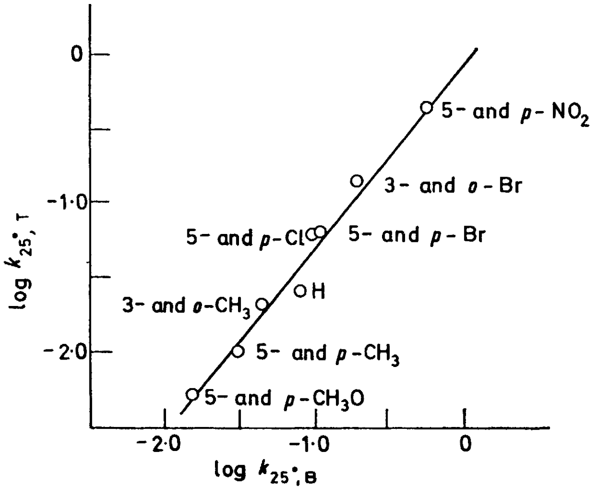

FIGURE 1 Plot of log $k_{25°}$ for the reactions of 3- and 5-substituted 2-thenoyl chlorides with aniline against log $k_{25°}$ for the reactions of the corresponding *ortho*- and *para*-substituted benzoyl chlorides with aniline

The plot of log *k* at 25° for the reactions of 3- and 5-substituted 2-thenoyl chlorides against log *k* at 25° for the reactions of corresponding *ortho*- and *para*-substituted benzoyl chlorides is linear with a slope of 1.27 (*r* 0.994) (Figure 1). This value is similar to that calculated from the ratio ρ : ρ′ = 1.26, where ρ is the reaction constant for the 5-substituted 2-thenoyl chloride reaction (1.79) [13] and ρ′ that for the *para*- and *meta*-substituted benzoyl chloride reaction (1.42).[14] A value higher than unity indicates that the thiophen nucleus is more efficient than the benzene ring in relaying the electronic effects of the substituents to the reaction centre.[13] The points for the 3- and *ortho*-derivatives lie close to the line indicating that a substituent in these positions, compared with the unsubstituted compounds

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[12] J. G. Mather and J. Shorter, *J. Chem. Soc.*, 1961, 4774.

[13] G. Alberghina, A. Arcoria, S. Fisichella, and G. Scarlata, *Gazzetta*, 1973, **103**, 319.

[14] R. A. Benkeser, C. E. DeBoer, R. E. Robinson, and D. M. Sauve, *J. Amer. Chem. Soc.*, 1956, **78**, 682.

and the 5- and *para*-derivatives, and in the transition state, compared with the initial state, does not exert steric strain or restriction in the rotation of the carbonyl chloride function.

A linear relationship was obtained between log *k* and the carbonyl stretching bands for the reactions of 2- and 3-thenoyl, 3-furoyl, and benzoyl chlorides.[4] Other examples of this correlation have been reported.[15,16] Tables 2 and 3 list the log *k* values at 25° for the reaction of substituted 2-thenoyl and benzoyl chlorides and the carbonyl i.r. stretching bands for CCl_4 solutions of the acid chlorides. A linear relationship is obtained plotting log *k* at 25° for the reactions of 3- and 5-substituted 2-thenoyl chlorides against the carbonyl stretching bands, except for 5-halogen-2-thenoyl chlorides (Figure 2), indicating that the same combination of factors is responsible for both the shift in carbonyl stretching frequency and the reactivity, although the i.r. carbonyl absorption is a property of the ground state only whereas the reactivity data refer to both ground and transition states. This linear relationship shows that the reactivity of the acid chlorides depends on the positive charge on the carbonyl carbon atom, that the rotation of the carbonyl chloride function in the transition state, compared with the initial state, for the unsubstituted acid chloride itself must be restricted, and that a methyl group or a bromine atom can be introduced into the 3-position in the thiophen ring without much steric strain and without much increase in the restriction of the rotation of the carbonyl chloride group.

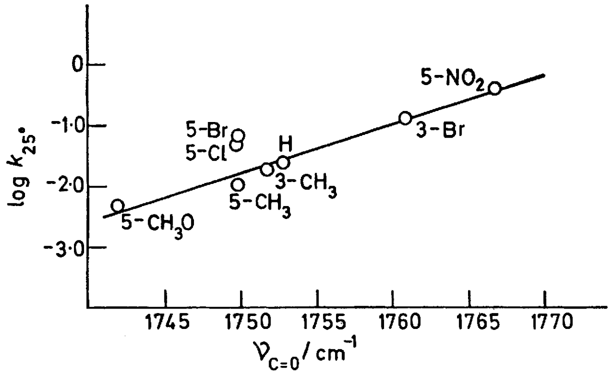

FIGURE 2 Plot of log $k_{25°}$ for the reactions of 3- and 5-substituted 2-thenoyl chlorides with aniline against the carbonyl stretching bands in CCl_4 of the acid chlorides

Recently, by use of simple Hückel MO theory for the reaction of 3- and 5-substituted 2-thenoyl chlorides with aniline, it was proposed that the substituent effect on the π-electron population of the carbonyl carbon atom is linearly related to the substituent effect on the reaction rate.[17] No relationship is obtained for benzoyl chlorides perhaps because of the complexity of the carbonyl band of these acid chlorides as noted by Forbes and Myron.[18]

EXPERIMENTAL

Materials.—3-Methyl-,[19] 3-bromo-,[20] and 5-bromo-2-thenoic acids[21] were prepared as reported. The acid chlorides were prepared as follows. Substituted 2-thenoic acid (5 g) was refluxed with thionyl chloride (15 ml) for several hours. The excess of thionyl chloride was removed by distillation in a water-bath and the acid chloride was purified by distillation under reduced pressure. 3-Methyl-2-thenoyl chloride had b.p. 216—217°,[22] 3-bromo-2-thenoyl chloride b.p. 135—136° at 13 mmHg,[23] and 5-bromo-2-thenoyl chloride b.p. 126° at 14 mmHg.[22] *ortho*- and *para*-Substituted benzoyl chlorides (Aldrich) and aniline (Carlo Erba) were distilled twice at reduced pressure.

I.r. spectra of acid chlorides were measured with a Perkin-Elmer 237 spectrometer using cells of 0.1 mm thickness. The solvent was CCl_4 (spectroscopic grade). Benzene (R. P. Carlo Erba) was used as solvent.[1]

Kinetic Measurements.—The reaction was followed kinetically, as previously,[3] by filtering the completely insoluble aniline hydrochloride, dissolving it in water and estimating the chloride with 0.01N-mercury(II) nitrate, using diphenylcarbazone as indicator, in the presence of Bromophenol Blue.

The second-order rate constants were calculated with constant molar ratios of the reactants: 1 equiv. of acid chloride and 2 equiv. of aniline, in agreement with equation (1). For bromo-derivatives the initial concentrations of the reactants after mixing were: acid chloride 0.002 5M, aniline 0.005M, for methyl derivatives acid chloride 0.005M, aniline 0.01M. All compounds gave excellent second-order kinetics. All reactions were performed in duplicate to at least 75—80% completion with <3% deviation between the two rate constants. Rate constants were calculated by a least-squares computer program using a Hewlett–Packard 9100 B computer. Activation parameters were calculated from a least squares treatment of log *k* against T^{-1}.

Product Analysis.—Standard solutions of the appropriate acid chloride (1 equiv.) and aniline (2 equiv.) in benzene were placed in a glass-stoppered bottle and maintained at the kinetic temperature until completion of the reaction. After concentration of the solution, the precipitated anilide (95% yield) was filtered off, washed free from aniline hydrochloride with water, dried, and recrystallized from ethanol. *3-Methyl-*N*-phenylthiophen-2-carboxamide* had m.p. 126° (Found: C, 66.15; H, 5.0; N, 6.3; S, 14.7. $C_{12}H_{11}NOS$ requires C, 66.35; H, 5.1; N, 6.45; S, 14.75%). *3-Bromo-*N*-phenylthiophen-2-carboxamide* had m.p. 74—75° (Found: C, 46.75; H, 2.8; Br, 28.4; N, 4.85; S, 11.3. $C_{11}H_8BrNOS$ requires C, 46.8; H, 2.85; Br, 28.3; N, 4.95; S, 11.35%).

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5-*Bromo*-N-*phenylthiophen*-2-*carboxamide* had m.p. 119° (Found: C, 46.8; H, 2.9; Br, 28.25; N, 4.9; S, 11.3. $C_{11}H_8BrNOS$ requires C, 46.8; H, 2.85; Br, 28.3; N, 4.95; S, 11.35%). Known anilides are benzanilide, m.p. 162°;[24] 2-methylbenzanilide, m.p. 125°;[25] 4-methylbenzanilide, m.p. 145°;[24] 2-bromobenzanilide, m.p. 123—124°;[26] and 4-bromobenzanilide, m.p. 197°.[27]

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