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Reactivity of 2-Halogenothiazoles towards Nucleophiles: Kinetics and Mechanisms of the Reactions of 2-Halogeno-X-thiazoles with Benzenethiolate lon

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The reactions between 4- and 5-X-substituted 2-chlorothiazoles and the benzenethiolate ion in methanol have been kinetically investigated. The aza-activation in 2-chlorothiazole is much reduced with respect to the commonly observed aza-activation in 6-membered cyclic aromatic derivatives. The substituent effect can be correlated with a Hammett relation when the 2,4- and 2,5-positions are considered as meta- and para-like respectively.

The high ρ value (+5.3) and the high experimental σ^- value for the ρ -NO₂ group (ca. 1.6) indicate that the thiazole system is very sensitive to the effect of the substituent. This is connected with the small delocalisation of the negative charge in the transition state in the penta-atomic ring.

THE quantitative aspects of the reactivity of heteroaromatic compounds are of interest.¹⁻³

We have been studying the reactivity of penta-atomic heterocyclic compounds having two or more heteroatoms.⁴ We now report on the reactions between 2halogenothiazoles X-substituted in position 4 and 5 $(X = H, Me, Ph, Cl, or NO_2)$ and benzenethiolate ion in methanol. Such a reaction can give information on the heteroaromatic nucleophilic reactivity, and also on the transmission of the electronic effect of the substituents through the thiazole ring. On the latter subject Imoto and his co-workers⁵ reported quantitative data concerning the acidity of X-substituted carboxythiazoles and the hydrolysis of the corresponding esters. Metzger and his co-workers⁶ extensively studied the reactivities of thiazoles, but their aims and reactions differ from ours.

RESULTS

Kinetic constants for the benzenethiolate dehalogenation in methanol are not easily determined since in this solvent, the reactive species (benzenethiol and methoxide ion) are also present [equilibrium (1)]. The reactions studied were (2)--(4), where C₃H₃NS is thiazole. All the reactions

$$PhS^{-} + MeOH \Longrightarrow PhSH + MeO^{-}$$
 (1)

 $2-\text{Cl}\cdot\text{C}_{3}\text{H}_{2}\text{NS} + \text{MeO}^{-}$

$$2\text{MeO} \cdot \text{C}_3\text{H}_2\text{NS} + \text{Cl}^- \quad (k_2) \quad (2)$$

2-Cl·C₃H₂NS + PhSH \longrightarrow

$$2-\text{PhS}\cdot\text{C}_{3}\text{H}_{2}\text{NS} + \text{H}^{+} + \text{Cl}^{-} \quad (h_{3}) \quad (3)$$
$$2-\text{Cl}\cdot\text{C}_{3}\text{H}_{2}\text{NS} + \text{PhS}^{-} \longrightarrow$$

$$\frac{2-PhS\cdot C_{2}H_{3}NS + Cl^{-}(k_{4})}{2}$$

$$k_{\text{total}} = k_2 [\text{MeO}^-] + k_4 [\text{PhS}^-]$$
(5)

follow a second-order kinetic law. For some substrates the rates of processes (2)-(4) are comparable, but for the chloronitro-derivative and the dichloro-derivatives, the reactivity with undissociated benzenethiol (determined independently) appears to be considerably lower than that observed with benzenethiolate ion. [Similar reactions

¹ A. R. Katritzky and S. M. Weds, Adv. Heterocyclic Chem., 1966, 7, 225. ² H. H. Jaffé and H. Lloyd Jones, Adv. Heterocyclic Chem.,

1964, 3, 209.

 ¹ G. Illuminati, Adv. Heterocyclic Chem., 1964, 3, 285.
 ³ G. Illuminati, Adv. Heterocyclic Chem., 1964, 3, 285.
 ⁴ P. E. Todesco, Bolletino, 1965, 23, 107; M. Foă, A. Ricci, P. E. Todesco, and P. Vivarelli, Bollettino, 1965, 23, 89; D. Dal Monte, E. Sandri, L. Di Nunno, S. Florio, and P. E. Todesco, Chem. Science and Construction of the con Chimica e Industria, 1969, 51, 987.

were recently reported by Illuminati and his co-workers 7 on the chloroquinolines, and by Vivarelli and Ricci⁸ on the 2-halogenobenzimidazoles.] The rate constants of process (3) are in Table 1.

TABLE 1

Kinetic constants of the reactions between 2-chloro-Xthiazoles and benzenethiol in methanol at 50 °C; [thiazole] = 0.01 M; [benzenethiol] = 0.5 M

 $X = 10^{6}k/$ 4-Cl 5-Cl 5-NO₂ 4-Me 4-Ph н 5-Me 3 0.31 10 $\mathbf{5}$ 9 6 l mol⁻¹ s⁻¹

The rate constant for process (4) has been measured in the presence of a small excess of free thiophenol so that the methoxide-ion concentration is negligible.

However, for X = 4-Ph, 4-Me, 5-Me, and H, the rates with benzenethiol and with benzenethiolate ion are similar and comparable with the rates of methoxide dehalogenation. For these substrates, the reactions were carried out in the presence of a large excess of the two reactive species (benzenethiolate and methoxide ions), *i.e.*, in pseudo-firstorder conditions with respect to the thiazole substrate. In these conditions equation (5) is valid, where k_{total} is the experimental constant (in s^{-1}) for the overall process of pseudo-first order, k_2 and k_4 are second-order constants for the two independent processes, [MeO⁻] and [PhS⁻] are initial concentrations of the two reagents, which remain virtually unchanged throughout the reaction; k_2 is determined from independent experiments.

Rates for the highly reactive 2-chloro-5-nitrothiazole were obtained by using a Gibson-Durrum stopped flow apparatus.

With thiazoles not substituted in position 5, the methoxide ion can attack the hydrogen ⁹ as in reaction (6). The value

$$\left(\begin{array}{c} N \\ S \end{array} \right) + Hal + MeO^{-} \xrightarrow{k_{-H}} \left(\begin{array}{c} N \\ K_{H} \end{array} \right) + Hal + MeOH \quad (6)$$

of $k_{-\rm H}/k_{\rm H}$ is very small since $k_{\rm H} \gg k_{-\rm H}$, and consequently the equilibrium will lie well to the left in methanol. Further,

⁵ Y. Otsuji, T. Kimura, Y. Sugimoto, E. Imoto, Y. Omori, and T. Okawara, Nippon Kagaku Zhasshi, 1959, 80, 1021, 1024; (Chem. Abs., 1960, 54, 24,796; 1961, 55, 5467).

⁶ R. Phan Tan Luu, L. Bouscasse, E. J. Vincent, and J. Metzger, Bull. Soc. Chim. France, 1969, 1149.
 ⁷ G. Illuminati, P. Linda, and G. Marino, J. Amer. Chem.

Soc., 1967, **89**, 3521.

A. Ricci and P. Vivarelli, J. Chem. Soc. (B), 1968, 1280.

⁹ R. A. Olofson, J. M. Landesberg, and K. N. Houk, J. Amer. Chem. Soc., 1966, 88, 4265; R. A. Coburn, J. M. Landesberg, Commun. 2007 (2007) 1998 (2007) 1998 (2007) 2007

D. S. Kemp, and R. A. Olofson, Tetrahedron, 1970, 26, 685.

we have not observed kinetic isotope effects in the methoxydechlorination of 2-chloro-5-deuteriothiazole, and we think that hydrogen exchange in position 5 is an independent process which does not affect the concentrations of the reactants.

TABLE 2

Arrhenius parameters for reactions of 2-chlorothiazole or 2-chloro-5-nitrothiazole with sodium benzenethiolate in methanol

2-Chlorothiazole

ſemp./	k	E_{a} /		ΔS^{\ddagger}
°Cົ່	l mol ⁻¹ s ⁻¹	kcal mol ⁻¹	$\log A/s^{-1}$	cal mol-1 K-1
25	0.27×10^{-6}		0 1	
35	0.79×10^{-6}			
50	$4.5 imes 10^{-6}$	21.6	9.3	18.3
2-Chlor	o-5-nitrothiazo	ole		
- 32.5	1.2			
-21.0	$5 \cdot 2$			
21.6	150			
$29 \cdot 3$	230			
50	850 *	11.8	10.9	10.9

* Value extrapolated from the data at lower temperatures.

The kinetic data are in Table 2. [In a preliminary communication ¹⁰ a higher value of k_2 for the reaction of 2-chlorothiazole $(6.5 \times 10^{-6} \text{ l mol}^{-1} \text{ s}^{-1})$ was reported. The difference is due to the intervention of free benzenethiol which was not considered in the earlier work.] In all cases normal substitution products are obtained in satisfactory yields (90-95%) and no evidence of competitive ring-opening reactions, as recently reported in similar cases by Ilvespää,¹¹ has been found.

For the dichloro-derivatives we have observed that after long reaction periods, halogen production is greater than expected on the basis of monosubstitution and indicates some substitution of both halogen atoms.

TABLE 3

Substituent effects in the reaction between 2-chloro-Xthiazoles and sodium benzenethiolate in methanol at 50 °C

X	10 ⁵ k/l mol ⁻¹ s ⁻¹
5-NO,	85,000,000 *
4-C1	31
5-C1	12
4-Ph	0.52
н	0.45
4-Me	0.16
5-Me	0.063
From	Table 2.

Recently Metzger reported ¹² that 4-chlorothiazole reacts with ethoxide ion in ethanol more slowly than the corresponding 2-chloro-isomer. Olofson and his co-workers⁹ have also reported that H-D exchange occurs at about the same rate at positions 2 and 5 of the thiazole in either CH₃OD or in D₂O with the corresponding base. We have also extensively investigated the reactivity of halogeno-thiazoles with some common nucleophiles.13

¹⁰ M. Foă, A. Ricci, and P. E. Todesco, Bollettino, 1965, 23, 229; G. Bartoli, L. Di Nunno, L. Forlani, and P. E. Todesco, Internat. J. Sulfur Chem., in the press. ¹¹ A. O. Ilvespää, Helv. Chim. Acta, 1968, **51**, 1723.

¹² J. Metzger, Recherches recentes dans la serie du 1,3-thiazole. J. Merger, Recherches fecences dans la serie du 1,3-thiazole.
 Invited lecture at the deuxieme Congrès International de Chimie Heterocyclique, Montpellier 7—11 Julliet 1969.
 ¹³ M. Bosco, L. Forlani, and P. E. Todesco, presented at IV Symposium on Organic Sulphur, Venice, June 15—20th, 1970.
 ¹⁴ M. Mongrini and C. Exponential Construction 1020, 2020.

14 A. Mangini and G. Frenguelli, Gazzetta, 1939, 69, 86.

In the case investigated here, g.l.c. of the reaction mixture carried out up to 70-80% of completion (as revealed by the production of free halide ion) showed the formation of only one product, in practically quantitative yields, which was identified as a 4-chloro-2-thiophenoxythiazole or 5chloro-2-thiophenoxythiazole depending on the substrate material. The data concerning the substituent effect are in Table 3.

DISCUSSION

In principle 2-halogenothiazoles can be considered as halogenoaromatic derivatives in which the aza-substituent exerts an activating power, similar to the $C-NO_2$ group. This was pointed out first by Mangini¹⁴ and later confirmed by several authors.¹⁵

A reaction pathway (7) similar to the commonly accepted aromatic bimolecular two-stage mechanism ¹⁶ (in which the formation of the intermediate is the ratedetermining step) can be postulated $(k_6 \gg k_5, k_{-5};$ class B in Bunnett's classification ¹⁷). This assumption can be

$$\underbrace{ \left(\begin{array}{c} N \\ S \end{array} \right)}_{N} Hal + Nu \xrightarrow{k_{5}}_{k_{-5}} \underbrace{ \left(\begin{array}{c} N \\ S \end{array} \right)}_{Nu} Hal \xrightarrow{k_{6}}_{Nu} \underbrace{ \left(\begin{array}{c} N \\ S \end{array} \right)}_{Nu} Hal \xrightarrow{k_{6}}_{Nu} Hal \xrightarrow{k_{7}}_{Nu}$$

made on the basis of the following points: (a) clean second-order kinetics, first order in both reactants; (b) dependence of the rates of the nature of the nucleophile; and (c) leaving-group effect indicating no bondbreaking in the transition state.

We have reported ¹⁰ the following sequences for the leaving group. For benzenethiolate F > I > Br > Cland for methoxide $F \gg Cl \sim Br > I$. Reaction (7) requires that substituents in the thiazole ring markedly affect the rate. Since the intermediate carries a negative charge, electron-withdrawing substituents, especially if present in a conjugated position, should increase the rate, while electron-releasing groups should decrease it. These conditions are verified in our case, as in passing from 2-chloro-5-methylthiazole to 2-chloro-5-nitrothiazole, an increase of 10⁹ rate units is observed. The observed variation of the rate with the substituent depend on the type of substituent and on its position in the thiazole.

All the data in Table 1 with the exception of those for the 5-nitro-derivative can be linearly correlated (r =0.9980; slope -0.24) with the data reported previously ¹⁸ for the oxidation of 2-phenylsulphinyl-X-thiazoles to the corresponding 2-phenylsulphonyl derivatives. The slope of the free-energy relationship is negative, as expected,

¹⁸ M. Bosco, L. Forlani, D. Sapone, and P. E. Todesco, Bollettino, 1969, 23, 83.

¹⁵ J. F. Bunnett and R. H. Zahler, *Chem. Rev.*, 1951, **49**, 273; J. Miller, 'Aromatic Nucleophilic Substitution,' in 'Reaction Mechanism in Organic Chemistry,' by C. Eaborn and N. B. Chapman, Elsevier Publ. Co., London, 1968, vol. 8, 234; F. Pietra, Quart. Rev., 1969, 23, 304.

 ¹⁶ J. F. Bunnett, *Quart. Rev.*, 1958, **12**, 1; A. J. Kirby and
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 and R. H. Garst, J. Amer. Chem. Soc., 1965, **87**, 3879; C. R.
 Hart and A. N. Bourns, Tetrahedron Letters, 1966, 2995.
 ¹⁷ J. F. Bunnett and J. D. Bordell, J. Amer. Chem. Soc. 1969.

¹⁷ J. F. Bunnett and J. D. Randall, J. Amer. Chem. Soc., 1958, 80, 6ŏ20.

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since the two reactions considered here have opposite electronic requirements.

Naturally, in the oxidation the electronic effects are less important than in the nucleophilic substitution, since in the former the attack is at the sulphur in a sidechain and the thiazole ring bearing the substituent is not directly involved as in the latter case. The p values observed for the oxidation of X-aryl sulphoxides to the corresponding sulphones 18,19 range between -0.4 and -0.7.

The large deviation of the 5-nitro-derivative from linearity probably originates from the greater influence of resonance effect (-M) in nucleophilic aromatic substitution than in oxidation reactions. In other cases of reactions at sulphur centres, σ -p-NO₂ is reported as close to unity.19,20

All the data for benzenethiolate substitution, except those of the 2-chloro-5-nitro-derivative, fit a Hammett type relationship (r = 0.9879; $\rho = 5.30$).²¹ The 4- and 5-positions are considered as 'meta-' and 'para'-like positions, and normal σ values as tabulated by McDaniel and Brown ²² are used. The ρ value is higher than that reported by Brieux 23 for the same reactions of 1-chloro-2-nitro-X-benzenes, indicating that the thiazole ring is more sensitive to the substituent effect.

The present results, and the previous data for the oxidation, clearly indicate that the simple Hammett equation is valid for the thiazole system, in agreement with similar conclusions for other penta-atomic rings.²⁴

Sophisticated multiparameter treatments of the data (Yukawa-Tsuno,²⁵ Taft ²⁶) are not justified in our case owing to the small number of substituents considered. The simple Hammett treatment is satisfactory with the exception of nucleophilic substitution of the nitroderivative and this is discussed below.

From the kinetic data and a p value for 2-chloro-5nitrothiazole, a σ^- value for the $p\text{-NO}_2$ group can be calculated. This value is unusually high 27 and indicates exceptional activation induced by the nitro-group. This exceptional activating power of the nitro-group in a penta-atomic cycle is not unique. For example it is well known that in hexa-atomic rings aza-activation and nitro-activation lie within one or two orders of magnitude, $k_{\rm nitro}/k_{\rm aza}$ being between 100 and 1.28

In our system the comparison between aza- and nitroactivation can be made by comparing the data for the reaction of 2-chloro-3-nitrothiophen with that for 2chlorothiazole (Table 4). The activating power of the aza-group is clearly shown, as 2-chlorothiophen is

¹⁹ G. Modena and P. E. Todesco, Bollettino, 1965, 28, 31; A. Cerniani and G. Modena, Gazzetta, 1959, 89, 843.

²⁰ G. Modena and L. Maioli, *Gazzetta*, 1957, 67, 1906.
 ²¹ L. P. Hammett, 'Physical Organic Chemistry,' McGraw-Hill Book Co., New York, 1940, p. 188.
 ²² L. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, 23, 400

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²³ A. M. Porto, L. Altieri, A. J. Castro, and J. A. Brieux, J. Chem. Soc. (B), 1966, 963.

 ²⁴ D. Spinelli and C. Dell'Erba, Tetrahedron, 1965, 21, 1061;
 G. Marino, Atti Accad. naz. Lincei Rend. Classe Sci. fis. mat. nat., 1965, 38, 700 (Chem. Abs., 1966, 64, 1917a); A. R. Butler and J. B. Hendry, J. Chem. Soc. (B), 1970, 848.

virtually unreactive in the conditions used here. The aza-activation in this case is low in comparison with the activating power of the C-NO₂ group. This is clearly indicated by the high reactivity ratio, k for the reaction of 2-bromo-3-nitrothiaphen with PhS⁻ being 2.4×10^5 times that for the reaction of 2-chlorothiozole. This contrasts sharply with the previous statement. [Comparison between a chloro- and a bromo-derivative is justified in this case as the chlorine : bromine ratio is three or less for halogenonitrothiophens²⁹ and 2halogenothiazoles.]

TABLE 4

Kinetic data of some reactions between benzene thiolate and halo-derivatives in methanol at 50 °C

			$\Delta S \ddagger$	
Derivative	k/l mol ⁻¹ s ⁻¹	$E/\text{kcal mol}^{-1}$	cal mol ⁻¹ K ⁻¹	Ref.
2-Chlorothiophen	a	·		b
2-Chlorothiazole	$4.5 imes10^{-6}$	22	-14.2	ь
2-Bromo-5-nitro- thiophen	ء ١٠١	13.8	-15.8	

^a Practically unreactive in the experimental conditions used here. ^b This work. ^c Data calculated by means of Arrhenius parameters reported in ref. 29.

The low aza-activation compared with the nitroactivation observed for the thiazole derivative may be due to the more efficient delocalisation of the negative charge in the transition state with a six-membered ring than that with a five-membered ring. Presumably the transition state has a structure near the intermediate Meisenheimer-like compound. [Meisenheimer-like compounds were recently detected in the case of nitrothiophens,³⁰ and this confirms that the addition-elimination mechanism $S_{N}Ar$ is also valid for heterocyclic derivatives.]

For these reasons the activating power of the nitrogroup, which can remove the negative charge from the ring, is more efficient in the five-membered ring than in the six-membered ring, as verified by us for 2-bromo-3nitrothiophene with respect to both 2-chlorothiazole and 2-chloro-5-nitrothiazole.

Conclusion.—We have shown that the simple Hammett equation can be applied satisfactorily to thiazole derivatives if positions 4 and 5 are considered as *meta*and *para*-like with respect to position 2. All the data concerning the nucleophilic substitution of 2-chlorothiazoles indicate that it is possible to consider a typical two-stage mechanism, $S_{\rm N}$ Ar, as a reaction pathway. Nitro-activation in the five-membered ring is much more efficient than aza-activation, because the nitro-substituent, if present in a conjugated position, effectively removes negative charge from the ring.

25 T. Tsuno, T. Ibata, and Y. Yukawa, Bull. Chem. Soc. Japan, 1959, 32, 965.

 ²⁶ R. Taft and I. C. Lewis, J. Amer. Chem. Soc., 1959, 81, 5343.
 ²⁷ H. Van Bekkum, P. E. Verkade, and B. M. Wepster, Rec. Trav. chim., 1959, 78, 815.

²⁸ Ref. 3, p. 319.

²⁹ D. Spinelli, C. Dell'Erba, and G. Guanti, Ann. Chim. (Italy), 1965, 52, 1252.

³⁰ G. Doddi, G. Illuminati, and I. Stegel, Chem. Comm., 1969, 953.

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EXPERIMENTAL

Kinetic Measurements.—The experiments were performed as described ³¹ by following the appearance of chloride ion (Volhard). With the reactions of 2-chloro-5-nitrothiazoles carried out at higher temperatures, rate coefficients were determined by using a Durrum-Gibson stopped-flow instru-

was crystallised from the appropriate solvent if solid, or distilled if liquid. While the conversion yields are in all cases higher than 95%, the yields of purified products are in some cases less (Table 5) owing to the high volatility of some thiazole derivatives.

In the case of the 2,4-dichlorothiazole, where substitution of both the chlorine atoms may occur, reaction is carried

TABLE 5

2-Phenylthio-X-thiazoles

		Found/%						Required/%					
x	B.p./mm.	Yield/%	C	H	N	S	Cl	Formula	C	н	N	S	CI
н	145/3 •	75						C.H.NS.					
4-Me	150/2	55	58.1	4 ·4	6.6	30.1		C, H, NS,	57.93	4.37	6.75	30.94	
5-Me	112/3	67	58.5	4.4	6.7	30.1		C ₁₀ H ₉ NS ₂	57.93	4.37	6.75	30.94	
4-Cl	48 5	100	47.4	2.5	6.1	28.6	15.9	C,H,NS,Cl	47.46	2.65	6.15	28.16	15.57
5-Cl	124/3	79	47.8	2.7	6.1	27.8	$15 \cdot 1$	C, H, NS, Cl	47.46	2.65	6.15	28.16	15.57
4-Ph	45 0	70	66.1	4 ·1	$5 \cdot 1$	$23 \cdot 4$		C15H11NS,	66.88	4.12	$5 \cdot 20$	$23 \cdot 80$	
5-NO ₂	97 0	90						$C_9H_6N_2O_2S_2$					

Picrate, m.p. 153°. M.p. (from light petroleum).

ment. The appearance of 5-nitro-2-phenylthiothiazole was followed by measuring the u.v. absorption at 355 nm (e 25,800). Care was taken to exclude oxygen from all mixtures.

Analytical grade methanol was purified by a standard method and distilled under nitrogen through a 1 m column packed with Fenske helices.

Substrates .--- 2-Chlorothiazole, b.p. 145°/760 mm; 32 2,4dichlorothiazole, m.p. 46° (from ethanol-water, 1:1); 33 2,5-dichlorothiazole, b.p. 160°/760 mm; 33 2-chloro-5-nitrothiazole, m.p. 64° (from light petroleum); 32 2-chloro-5-

out until development of halogen-ion has reached 70% for monosubstitution (ca. 3 h at 50 °C with concentrations reported above). The crude residue obtained from evaporation of ethereal extracts is easily separated by column chromatography.

Unchanged 2,4-dichlorothiazole (0.29 g, 0.0019 mol, 29% yields) and 4-chloro-2-phenylthiothiazole (1.04 g, 0.0046 mol, 71% yield) were obtained and identified by n.m.r. and i.r. spectra and by elemental analysis.

Analogous results were obtained in the case of 2,5-dichlorothiazole.

TABLE 6

Spectral data (i.r. and n.m.r.) of 2-phenylthio-X-thiazole

			-				•		N.m.r. m	easurement	(in CCl ₄)
X = I.r. measurement in Nujol (N) or neat film (F)									τ _{H(4)}	$\tau_{\mathbf{H}(4)}$	тмe
н	(F)	1579m		1472s	1438s	1381s	1300s		2.42	2.90	
4-Me	(F)	1578m	1520s	1472s	1438s	1407s	1370s			3.37	7.66
5-Me	(F)	1578m	1528w	1475s	1438s	1405s	1300w		2.5		7.66
4-Cl	(N)	1569w			1438m		1302w			3.18	
5-C1	(F)	1578m	1484s	1472s	1438s	1393s	1300w		2.67	_	
4-Ph	(Ń)	1595w	1575w		1436s	1411s	1318w	1302w		2.80	
$5-NO_2$	(N)	1570w	1503s		1430m		1330s		1.88		-
					a .						

s = Strong, m = medium, w = weak.

methylthiazole, b.p. 166°/760 mm; 34 2-chloro-4-methylthiazole, b.p. 60°/20 mm; 35 and 2-chloro-4-phenylthiazole, m.p. 54° (from ethanol),36 were obtained by known procedures.

Reaction Products.—The products were determined by operating in conditions similar to those used during the measurements, as follows: thiazole-derivative (1.0 g,0.0065 mol) in CH₃OH (20 ml) was added to a methanol solution of $C_6H_5S^-$ (20 ml of 1M-solution) containing a small excess of free benzenethiol. When the reaction was nearly completed (as revealed by chloride-ion analysis), the reaction mixture was poured on ice-water, neutralised, and extracted with ether.

Evaporation of the extract gave a crude product which

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101. ³² K. Ganapathi and A. Venkataraman, Proc. Indian Acad. ¹⁰⁴⁶ 40 4059). Sci., 1945, 22, A, 370 (Chem. Abs., 1946, 40, 4059).
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France, 1962, 1736.

The i.r. spectra are recorded by a Perkin-Elmer spectrometer, model 257; the absorption bands near 1610, 1500, and 1380 cm⁻¹ were described by Katritzky and his coworkers ³⁷ as typical of the thiazole ring.

The n.m.r. spectra were recorded with a Varian 100 MHz instrument with tetramethylsilane as internal standard. The protons which fall at $\tau 2.4$ and 2.7 (in this region the signals of aromatic protons are present as a broad multiplet) were assigned by decoupling of the aromatic protons.

Data for all the products are in Tables 5 and 6.

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 ³⁶ G. Vernin and J. Metzger, Bull. Soc. chim. France, 1963, 2498.

³⁷ A. R. Katritzky, Quart. Rev., 1959, 13, 353.