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STUDIES IN HETEROCYCLIC CHEMISTRY—I

THE FORMATION OF BENZOTHIAZOLES FROM N,S-DIACYL *o*-AMINOTHIOPHENOLS

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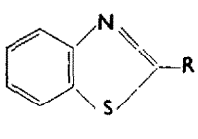
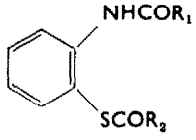
Abstract—The partial hydrolysis of N,S-diacyl *o*-aminothiophenols yields *o*-amidothiophenols which are quantitatively converted to benzothiazoles. Hydrolysis of the thiol ester grouping is facilitated by anchimeric assistance from the adjacent amido grouping, leading first to the isomeric N,N-diacyl derivative which subsequently undergoes rapid hydrolysis. Analysis of the mixture of benzothiazoles formed from mixed N,S-diacyl derivatives by this migration suggests that participation of this type occurs generally in such systems. The efficiency with which the internally assisted hydrolysis competes with external hydrolysis is dependent on the nature of the acyl groups and the aminothiophenol.

THE formation of benzazole ring systems by the action of acylating agents on the appropriate *o*-substituted aniline provides a convenient route to these compounds. Benzimidazoles can be obtained directly from the action of carboxylic acids on *o*-phenylene diamines but benzoxazoles and benzothiazoles are usually prepared by the partial hydrolysis of the corresponding diacyl derivatives. Thus 2-phenylbenzothiazole (I) is readily obtained from the dibenzoyl derivative (II, $R_1 = R_2 = C_6H_5$). During an investigation of this reaction Lankelma and Knauf[1] noted that from the isomeric



I



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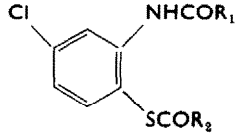

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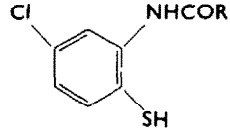


IV

S-benzoyl-N-acetyl and S-acetyl-N-benzoyl derivatives of 2-amino-4-chlorothiophenol the product was in each case 5-chloro-2-phenylbenzothiazole. In an attempt to elucidate the mechanism of this reaction and the rearrangement implicit in these results a number of related N,S-diacyl aminothiophenols have been prepared and a study made of their subsequent decomposition.

The reduction of 4,4′-dichloro-2,2′-dinitrodiphenyldisulphide provides a convenient route to 2-amino-4-chlorothiophenol. The use of a variety of reducing agents has been reported—zinc and acetic acid,[2,3] tin and hydrochloric acid,[1] aqueous sodium sulphide.[4] In our hands satisfactory results were obtained only with sodium sulphide. The thiophenol is unstable, rapidly decomposing on exposure to atmospheric oxygen

[1] H. P. Lankelma and A. E. Knauf, *J. Amer. Chem. Soc.* **53**, 309 (1931).
[2] J. Pollack, E. Riesz and Z. Kahane, *Monatsh.* **49**, 213 (1928).
[3] K. J. Farrington and W. K. Warburton, *Austral. J. Chem.* **8**, 545 (1955).
[4] H. Hauser, *Helv. Chim. Acta* **11**, 198 (1928).

yielding the alkali insoluble disulphide. This rapid oxidation may well be responsible for the widely divergent physical properties recorded for the thiophenol.[1-5]

The diacetyl (III, $R_1 = R_2 = CH_3$) and dibenzoyl (III, $R_1 = R_2 = C_6H_5$) derivatives of 2-amino-4-chlorothiophenol were prepared and had the properties described by Lankelma and Knauf.[1] The IR spectra (Table 1) showed those characteristics expected for a thiolester and a secondary amide. On treatment with aqueous alcoholic alkali one acyl group was hydrolysed and the corresponding monoacyl derivative was

TABLE 1. BANDS IN THE I.R. SPECTRA OF N,S-DIACYL-O-AMINOTHIOPHENOLS

	Frequencies ($cm.^{-1}$)*				
	N—H	C=O			
		$N—COCH_3$	$N—COC_6H_5$	$S—COCH_3$	$S—COC_6H_5$
Acetanilide	3450	1705			
Benzanilide	—		1687		
Phenyl thiolacetate				1713	
Phenyl thiolbenzoate					1685
N,S-*diacyl-o-amino-thiophenols*					
S-acetyl, N-acetyl	3410	1710		1730	
S-benzoyl, N-benzoyl	3410		1660		1691
S-acetyl, N-benzoyl	3410		1690	1728	
S-benzoyl, N-acetyl	3410	1708			1692
N,S-*diacyl-2-amino-4-chlorothiophenols*					
S-acetyl, N-acetyl	3400	1715		1732	
S-benzoyl, N-benzoyl	3410		1693†		1693†
S-acetyl, N-benzoyl	3400		1693	1735	
S-benzoyl, N-acetyl	3400	1715			1693
N,S-*diacyl-o-methyl-aminothiophenols*					
S-acetyl, N-acetyl		1685		1714	
S-benzoyl, N-benzoyl			1657		1684

* Spectra measured for solutions in CS_2.

† Bands not resolved.

precipitated by cautious acidification. The solubility of these compounds in alkali—from which they can be reprecipitated—and their IR spectra showing bands characteristic of both mercapto and amide groups leave no doubt that they are correctly described as amidothiophenols (IV, $R = CH_3$, C_6H_5). Solutions of these monoacyl derivatives in neutral solvents undergo rapid and quantitative cyclization to the corresponding benzothiazoles. However, under basic conditions the solutions show much greater stability and acylation under such conditions allows the mixed N,S-diacyl compounds to be prepared. The two isomeric acetyl—benzoyl derivatives (III, $R_1 = CH_3$, $R_2 = C_6H_5$; $R_1 = C_6H_5$, $R_2 = CH_3$) were readily obtained in this way. The two compounds, stable to repeated crystallization, were readily distinguishable: their physical properties were similar to those described by Lankelma and Knauf.[1] Thin-layer chromatography revealed that the re-acylation reaction produced only one diacyl compound in each case and the IR spectra (Table 1) strongly suggest that the N-acyl residue does not migrate under these conditions.

[5] H. H. Hodgson and J. H. Wilson, *J. Chem. Soc.* 440 (1925).

Hydrolysis of the mixed N,S-diacyl compounds proceeded readily in dilute aqueous alcoholic alkali with the liberation of one equivalent of carboxylic acid. The product was immediately converted to benzothiazole. Examination of the resultant material showed that, in contrast to the findings of Lankelma and Knauf,[1] it was a mixture of the 2-methyl- and 2-phenylbenzothiazoles; thin-layer chromatography of the liberated acids revealed the complementary mixture of benzoic and acetic acids.

To explore the generality of this reaction the preparation and hydrolysis of several additional mixed and simple N,S-diacyl derivatives was undertaken. For convenience derivatives of *o*-aminothiophenol were used. The preparation and properties of the

TABLE 2. COMPOSITION OF BENZOTHIAZOLES FORMED FROM THE PARTIAL HYDROLYSIS OF MIXED N,S-DIACYL-O-AMINOTHIOPHENOLS

N,S-*diacyl*-o-*aminothiophenols*	Mols (%) 2-methyl-benzothiazole	2-phenyl-benzothiazole	Other 2-substituted benzothiazole
S-acetyl, N-propionyl	36		64[a]
S-propionyl, N-acetyl	38		62[a]
S-acetyl, N-benzoyl	62	38	
S-benzoyl, N-acetyl	62	38	
S-*m*-toluoyl, N-benzoyl		37	63[b]
S-benzoyl, N-*m*-toluoyl		5	95[b]
N,S-*diacyl*-2-*amino*-4-*chlorothiophenols*			
S-acetyl, N-benzoyl	25[c]	75[c]	
S-benzoyl, N-acetyl	39[c]	61[c]	

[a] 2-ethylbenzothiazole; [b] 2-(*m*-tolyl)-benzothiazole; [c] 2-substituted 5-chlorobenzothiazole.

N,S-diacyl compounds were closely similar to those of the 4-chloro analogues; characteristic bands in their spectra are recorded in Table 1. The hydrolyses were in all respects similar to those of the 4-chloro analogues, yielding first the N-acylaminothiophenol which could be characterized by its IR spectrum. The preparation of *o*-acetamidothiophenol by the action of acetic anhydride in acetic acid on *o*-aminothiophenol has been reported by Farrington and Warburton[3] but their product has properties differing largely from those of the compound obtained by hydrolysis. The reported properties correspond closely to those of the N,S-diacetyl derivative (II, $R_1 = R_2 = CH_3$) and careful analysis of the crude product from this acetylation revealed the presence of this compound together with much 2-methylbenzothiazole.

The monoacyl derivatives were either re-acylated or converted to the corresponding benzothiazoles. The crude benzothiazole product from the mixed N,S-diacyl compounds (II, $R_1 \neq R_2$) was in each case a mixture of the two possible compounds. Examination of the mixtures by thin-layer and gas-liquid chromatography and by IR and UV spectroscopic methods enabled them to be analysed (Table 2). No products other than the two benzothiazoles and the corresponding carboxylic acids were detected.

The formation of mixtures of benzothiazoles by the cyclization of the intermediate amidothiophenols requires that at least some of the acyl groups initially bonded to

sulphur have migrated to nitrogen. The possibility that the mixed N,S-diacyl derivatives can isomerize before hydrolysis occurs is excluded by the stability of these compounds under neutral conditions: repeated dissolution in ethanol leads to no isomerization. Similarly the possibility of isomerization during the re-acylation of the amidothiophenols can also be discounted for even under Schotten–Bauman conditions with benzoyl chloride *o*-acetamidothiophenol gave only the thiolbenzoate (II, $R_1 = C_6H_5$, $R_2 = CH_3$). Confirmation of this is provided by the pattern of carbonyl stretching bands in the IR spectra of the N,S-diacyl derivatives (Table 1) which indicates that no migration has occurred at this stage. Finally, experiment showed that, in accordance with expectation, no acyl exchange occurs between carboxylate ions and the N-acyl group. Consequently the recognition of the initial hydrolysis product as an amidothiophenol implies the occurrence of a sulphur to nitrogen acyl migration proceeding in competition with the hydrolysis of the thiol ester.

Acyl migrations of this type are well established for 2-aminoalkyl carboxylates[6] and thiolcarboxylates[7] which rearrange under alkaline conditions through a cyclic intermediate (V) to the 2-acylaminoalcohols and thiols. For the operation of this mechanism in the hydrolysis of the N,S-diacyl compounds it is necessary that the normally facile direct hydrolysis of the thiol ester be sufficiently retarded to allow liberation of a free amino group from the amide to be an effectively competing reaction. Similarly the analogous participation by the weakly nucleophilic amido group can only be effective in promoting S → N-acyl migration if the rate of direct hydrolysis of the thiol ester is reduced. Examples of such retardations are found in the influence of the steric and direct field effects of *ortho* substituents on the hydrolysis of phenyl esters.[8] Alternatively, enhancement of the ability of the amide group itself to participate in the reaction might lead to an increased rate of hydrolysis. Accordingly, the rates of hydrolysis of a number of N,S-diacyl *o*-aminothiophenols and some related compounds were determined.

The kinetic measurements were made under *pseudo*-first order conditions using an excess of base. Large differences in reactivity precluded the use of the same conditions for all the rate determinations. Thus phenyl thiolacetate is apparently unaffected by alcoholic sodium acetate solution whereas under similar conditions its *o*-acetamido derivative undergoes facile hydrolysis. However, by using different sets of reaction conditions inter-related series of relative rates were obtained (Table 3). The experimental results in all cases gave excellent first order plots suggesting, by analogy with other carboxylate hydrolyses,[9] that the reaction was second order overall.

It is immediately apparent (Table 3) that the hydrolysis of the N,S-diacyl compounds is particularly facile. Consequently the introduction of an *o*-acylamino substituent into a thiophenyl ester far from reducing the rate of hydrolysis markedly accelerates it. Only in the case of the N,S-dibenzoyl compound (which is discussed below) does the normal *ortho* effect become apparent. Further, the action of alkali

[6] L. H. Welsh, *J. Amer. Chem. Soc.* **69**, 128 (1947); **71**, 3500 (1949); A. P. Phillips and R. Baltzly, *Ibid.* **69**, 200 (1947); G. Fodor and J. Kiss, *Ibid.* **72**, 3495 (1950); E. E. van Tamelen, *Ibid.* **73**, 5773 (1951).

[7] R. B. Martin, S. Lowey, E. L. Elson and J. T. Edsall, *J. Amer. Chem. Soc.* **81**, 5089 (1959); R. B. Martin and A. Purcell, *Ibid.* **83**, 4830, 4835 (1961); R. B. Martin and R. I. Hedrick, *Ibid.* **84**, 106 (1962).

[8] C. K. Ingold, *Structure and Mechanism in Organic Chemistry* pp. 758, 759, Bell, London (1953).

[9] M. L. Bender, *Chem. Revs.* **60**, 53 (1960).

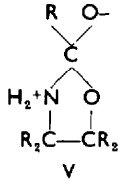
TABLE 3. RELATIVE RATES OF HYDROLYSIS OF THIOPHENYL ESTERS

	Reaction Conditions		
	10^{-2} N KOH	10^{-3} N KOH	10^{-1} N CH_3CO_2Na
Ester	16°	25°	25°
Phenyl thiolbenzoate	1·5		
Phenyl thiolacetate	13	1·0[b]	
Acylated o-amino-thiophenols			
N,S-dibenzoyl	1·0[a]		
N-methyl-N,S-dibenzoyl	5·7		
N-methyl-N,S-diacetyl	71	4·5	
N-acetyl-S-benzoyl			0·7
N-benzoyl-S-acetyl		38	1·0[c]
N,S-diacetyl			26
p-N,S-diacetyl	18[d]	0·9	

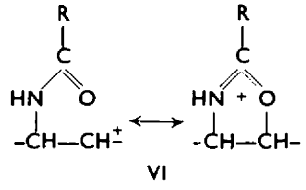
[a] $k_1 = 1{\cdot}3 \times 10^{-3}$ sec.$^{-1}$; [b] $k_1 = 2{\cdot}9 \times 10^{-2}$; [c] $k_1 = 3{\cdot}5 \times 10^{-5}$; [d] at 25°.

on *p*-acetamidothiophenyl acetate reveals that it, in accordance with the Hammett *sigma* constant[10] for *p*-$NHCOCH_3$ ($\sigma = 1{\cdot}0$), has a reactivity similar to that of thiophenyl acetate and less than that of the *ortho* isomer by a factor of 10^3. Consequently an explanation requiring anchimeric assistance of the hydrolysis is needed. The failure of the N-methyl derivatives to show an acceleration similar to that of the secondary amides suggests that the amino N–H function is an important factor in the reaction.

The ability of a neighbouring amide group to facilitate solvolytic cleavage of toluene sulphonate groups has been clearly demonstrated.[11] The interaction in such systems between the carbonyl group of the amide system and the incipient carbonium ion leads to a five-membered cyclic ion (VI). It is unlikely that the corresponding



V



VI

seven-membered cyclic system which could be formed by an analogous interaction in the N,S-diacyl compounds would lead to significant stabilization of the transition state; nor could such interaction readily account for the migration of an acyl group. An alternative mode of interaction of the amide group is available under conditions sufficiently basic to remove a portion from it. Thus in the presence of alkali, substituted succinimides are readily formed[12] from the corresponding amido esters (VII). Kinetic studies[13] have shown that the concurrent hydrolysis of the carboxylic ester is greatly accelerated by this interaction. The kinetic data are consistent with a reaction

[10] D. H. McDaniel and H. C. Brown, *J. Org. Chem.* **23**, 420 (1958).

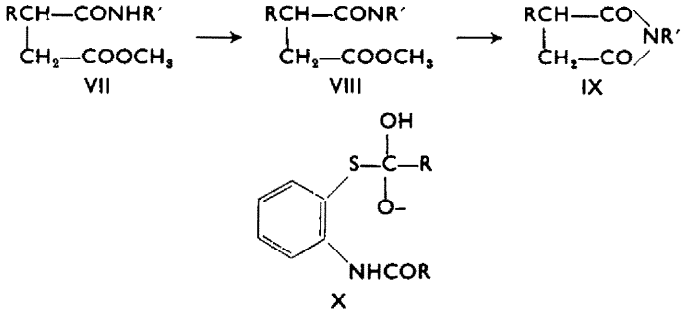
[11] G. E. McCasland, R. K. Clark and H. E. Carter, *J. Amer. Chem. Soc.* **71**, 637 (1949); S. Winstein and R. Boschan, *Ibid.* **72**, 4669 (1950).

[12] J. E. H. Hancock and R. P. Linstead, *J. Chem. Soc.* 3490 (1953); A. R. Battersby and J. C. Robinson, *Ibid.* 259 (1955); E. Sondheimer and R. W. Holley, *J. Amer. Chem. Soc.* 76, 2467 (1954).

[13] S. A. Bernhard, A. Berger, J. H. Carter, E. Katchalski, M. Sela and Y. Shalitin, *J. Amer. Chem. Soc.* **84**, 2421 (1962).

sequence in which the rate determining step involves loss of a proton from the amide group (VIII) and is followed by cyclization to the imide (IX).

The loss of a proton from the amide under the mildly basic conditions used for these reactions is surprising. The ability of intramolecular catalysis to provide a more



efficacious route than intermolecular catalysis may account for this. Thus the intermediate (X) formed by attack of an external nucleophile on the ester grouping is suitably orientated to abstract a proton from the amide. Additionally the product has the stereochemistry appropriate for anchimerically assisted hydrolysis of the ester and the consequent acceleration due to this process occurs in part from retardation of the direct hydrolysis.

With the exception of the N,S-dibenzoyl derivative (II, $R_1 = R_2 = C_6H_5$) the results obtained from the hydrolysis of the *o*-acylaminothiophenyl esters conform to the pattern expected from anchimeric assistance by the amide group. The acceleration in rate following introduction of the N-acyl group is in each case accompanied by S → N-acyl migration. Even with the N,S-dibenzoyl derivative, although the kinetic measurements give no indication of anchimeric assistance in the hydrolysis, the products from the closely related mixed benzoyl-*m*-toluoyl derivatives (II, R_1, $R_2 = C_6H_5$, *m*-$CH_3C_6H_4$) indicate that considerable migration does occur. The reason for the failure of the N,S-dibenzoyl derivative to show any increased activity becomes apparent from examination of molecular models. The rigidity derived from the accumulation of bulky groupings about the reaction centre, and in particular the effect of the *ortho* hydrogen atoms in the benzoyl groups, largely shields the ester carbonyl group from nucleophilic attack and reduces the accessibility of the amido group. Consequently in this compound a conventional *ortho* effect operates to reduce both the rate of direct hydrolysis of the ester and that of the amide-assisted reaction. In the corresponding N-methyl amide the molecule cannot adopt a fully planar structure and the steric inhibition of external nucleophilic attack is largely removed.

Some indication of the amount of anchimerically assisted hydrolysis can be obtained from the relative proportions of the two benzothiazoles formed from the mixed N,S-diacyl compounds. The results (Table 2) indicate that within the estimated accuracy (ca. 5%) the hydrolysis of the mixed acetyl—propionyl and acetyl—benzoyl derivatives of *o*-aminothiophenol proceeds entirely with the participation of the amide group. This result is in accord with the large acceleration in the rate of reaction. Conversely, the products from the mixed benzoyl–*m*-toluoyl derivatives suggest that a significant amount of direct hydrolysis does occur here. If the N,N-diacyl intermediates from the two isomers decompose in the same way (i.e. if their mean lifetime

is sufficient to permit rotational equilibration) then the product composition is consistent with up to a third of the hydrolysis following a non-assisted route.* It is noteworthy that even in this case when the overall reaction is slow the anchimerically assisted hydrolysis still accounts for the majority of the product. A similar analysis of the results for the mixed acetyl–benzoyl derivatives of 2-amino-4-chlorothiophenol suggests that ca. 15% of the reaction can proceed by direct hydrolysis. This significantly exceeds experimental error and is a clear departure from the pattern of the chlorine-free analogues. It is to be expected that the *para*-chloro substituent will increase the overall rate of hydrolysis of the thioester and decrease the effective participation of the amide group. Morawetz and Shafer[14] have shown that for related amide assisted hydrolyses the increase in acidity of the amide group following such substitution does not compensate for the reduction in its nucleophilicity. Consequently the direct hydrolysis is better able to compete with the anchimerically assisted reaction in these compounds.

The considerable variation in the proportions of phenyl and methylbenzothiazoles formed from the unsubstituted and chloro substituted analogues is also of interest. The possibility of interaction of the thiophenate ion with the N,N-diacyl system in the reaction intermediate is apparent in all these compounds (although the infrared spectra of the neutral N-acyl aminothiophenols show that they are correctly described as such). Such interaction will be subject to steric and electrical factors and will tend to retain within the molecule that acyl group presenting the most favourable configuration. The reduction in this interaction on the introduction of a *para*-chloro substituent may well account for the change in benzothiazole ratios.

EXPERIMENTAL

Preparation of 2-amino-4-chlorothiophenol

A suspension of 4,4′-dichloro-2,2′-dinitrodiphenyl disulphide (12 g) in water (66 ml) containing $Na_2S\ 9H_2O$ (30 g) was boiled under reflux for 3 hr. The resultant solution was chilled in an ice–salt bath and neutralized with 4N HCl aq. The thiophenol was extracted into ether (2 × 50 ml) and washed with water. The dried ethereal solution was filtered and treated with dry HCl giving 2-amino-4-chlorothiophenol hydrochloride (14 g), m.p. 196–200°. The free base was obtained as an oil by treatment of the hydrochloride with $NaHCO_3$ aq; on standing it rapidly decomposed to the disulphide, m.p. 115–116° (from ethanol).

Preparation of simple N,S-*diacyl* o-*aminothiophenols*

o-*Acetamidophenyl thiolacetate.* A solution of *o*-aminothiophenol (6·4 g) and acetic anhydride (12·7 g) in N,N-dimethylaniline (25 ml) was heated on a water bath for 10 min. The cooled solution was poured into cold 4N HCl aq (150 ml) precipitating the *diacetyl derivative* (6 g), m.p. 113–114° from water (Found: C, 57·2; H, 5·3; N, 6·9; S, 15·2. $C_{10}H_{11}NO_2S$ requires: C, 57·4; H, 5·3; N, 6·7; S, 15·3%).

Similarly prepared from *o*-aminothiophenol and the corresponding acid chlorides were the

* It is implicit in these results that the *m*-toluoyl residue is hydrolysed preferentially from the N,N-diacyl intermediate. If the amount of direct hydrolysis is the same for the two N,S-diacyl isomers, the *m*-toluoyl group is lost from the N,N-diacyl intermediate at a rate ca. twelve times that of the benzoyl group: whence ca. 32% of the product is derived from direct hydrolysis. However, it is possible that the amount of direct hydrolysis will also vary between the two isomers. The ratio *m*-toluoyl:benzoyl lost in direct hydrolysis is unlikely to exceed that operating for the N,N-diacyl compound. With this assumption the analytical data give a value of ca. eighteen for the ratio of rates and indicate 33% direct hydrolysis for the S-toluoyl isomer and 2% for the S-benzoyl isomer.

[14] J. A. Shafer and H. Morawetz, *J. Org. Chem.* **28**, 1899 (1963).

following compounds: o-*benzamidophenyl thiolbenzoate*, m.p. 158–159° from ethanol–benzene (Found: C, 71·9; H, 4·4; N, 4·6; S, 9·7. $C_{20}H_{15}NO_2S$ requires: C, 72·2; H, 4·5; N, 4·2; S, 9·6%); o-*propionamidophenyl thiolpropionate*, m.p. 66–67° from light petroleum–benzene (Found: C, 60·6; H, 6·2. $C_{12}H_{15}NO_2S$ requires: C, 60·7; H, 6·4%); o-(3-*toluamido*)-*phenyl thiol*-3-*toluate*, m.p. 98–99° from light petroleum-benzene (Found: C, 72·9; H, 5·3. $C_{22}H_{19}NO_2S$ requires: C, 73·1; H, 5·3%).

From *o*-methylaminothiophenol was obtained N-*methyl*-o-*acetamidophenyl thiolacetate* as an oil, b.p. 162°/2·5 mm, rapidly showing a pink coloration on exposure to air (Found: C, 59·2; H, 6·3. $C_{11}H_{13}NO_2S$ requires: C, 59·2; H, 5·9%); and N-*methyl*-o-*benzamidophenyl thiolbenzoate*, m.p. 128–129° from ethanol (Found: C, 72·4; H, 4·6. $C_{21}H_{17}NO_2S$ requires: C, 72·6; H, 4·9%).

From 2-amino-4-chlorothiophenol hydrochloride the N,S-diacetyl derivative, m.p. 149–150° from ethanol and the N,S-dibenzoyl derivative, m.p. 161–163° from benzene–ethanol were similarly prepared.

Acetylation of *p*-aminothiophenol in an analogous manner gave p-*acetamidophenyl thiolacetate*, m.p. 146–147° from aqueous ethanol (Found: C, 57·4; H, 5·3; S, 15·3%).

Preparation of N-*acyl* o-*aminothiophenols*

(i) o-*Acetamidothiophenol.* The yellow solution of *o*-acetamidophenyl thiolacetate (2·09 g, 10 mmoles) in aqueous 2N KOH (10 ml, 20 mmoles) was cooled and acidified with cold N H_2SO_4 aq (25 ml, 25 mmoles). The precipitate of *o*-acetamidothiophenol (1·6 g), m.p. 82–84° (dec) was collected; the I.R. spectrum of a mull with nujol showed absorption at 3220 cm^{-1} (N—H), 2532 cm^{-1} (S—H) and 1642 cm^{-1} (C=O). On standing the thiol (1·0 g) rapidly decomposed to 2-methylbenzothiazole (0·89 g, 99%).

Similarly prepared from the corresponding N,S-diacyl *o*-amino-thiophenols were the following compounds: *o*-benzamidothiophenol, m.p. 103–105° (dec); *o*-propionamidothiophenol, m.p. 45–46° (dec.). 2-Acetamido-4-chlorothiophenol and *o*-(3-toluoylamido)-thiophenol melted with decomposition over a wide temp range: from the latter 2-(*m-tolyl*)-*benzothiazole*, m.p. 63–64° from light petroleum–benzene was obtained (Found: C, 74·6; H, 5·1. $C_{14}H_{11}NS$ requires: C, 74·6; H, 4·9%).

(ii) *Attempted preparation of* o-*acetamidothiophenol*[8]. A solution of *o*-aminothiophenol (1 g) and acetic anhydride (1 g) in glacial acetic acid (3 ml) was allowed to stand for 5 min at 25°. The solution was poured over ice, treated with excess $NaHCO_3$, and the resultant solution extracted into ether. The product (1·1 g) was largely composed of 2-methylbenzothiazole, identified spectroscopically and chromatographically by comparison with an authentic specimen, but contained a minor component identified chromatographically as *o*-acetamidophenyl thiolacetate.

Preparation of mixed N,S-*diacyl* o-*aminothiophenols*

o-*Acetamidophenyl thiolbenzoate.* A solution of *o*-acetamidothiophenol (1·6 g) and benzoyl chloride (1·4 g) in N,N-dimethylaniline (5 ml) was heated on a water bath for 10 min. The cooled solution was poured into cold N HCl aq (100 ml) precipitating o-*acetamidophenyl thiolbenzoate* (1·7 g, 63%), m.p. 139–140° from aqueous ethanol. (Found: C, 66·4; H, 4·8; N, 5·1; S, 12·0. $C_{15}H_{13}NO_2S$ requires: C, 66·3; H, 4·8; N, 5·2; S, 11·8%).

Benzoyl chloride (1·6 g) was added to a solution of potassium *o*-acetamidothiophenate formed *in situ* by the action of 4N KOH aq (10 ml) on *o*-acetamidophenyl thiolbenzoate (2 g). The solid product which separated on shaking the mixture was collected. Thin-layer chromatography showed the presence of only *o*-acetamidophenyl thiolbenzoate.

The following compounds were prepared from solution in either dimethylaniline or pyridine of the appropriate *o*-acylaminothiophenol by the action of either acyl halide or anhydride: o-*benzamidophenyl thiolacetate*, m.p. 121–122° from aqueous ethanol. (Found: C, 66·2; H, 4·9; N, 5·3; S, 11·9%); o-*propionamidophenyl thiolacetate*, m.p. 101–101·5° from light petroleum–benzene. (Found: C, 59·2; H, 5·9. $C_{11}H_{13}NO_2S$ requires: C, 59·2; H, 5·9%); o-*acetamidophenyl thiolpropionate*, m.p. 74–75° from light petroleum–benzene. (Found: C, 59·0; H, 6·0%); o-(3-*toluoylamido*)-*phenyl thiolbenzoate*, m.p. 91–92° from light petroleum-benzene. (Found: C, 72·6; H, 4·8. $C_{21}H_{17}NO_2S$ requires: C, 72·6; H, 4·9%); o-*benzamidophenyl thiol*-m-*toluate*, m.p. 92–93° from light petroleum–benzene. (Found: C, 72·8; H, 5·2%): the mixed m.p. 58–67° of the last two compounds was depressed; 2-benzamido-4-chlorophenyl thiolacetate, m.p. 125–126°; 2-acetamido-4-chlorophenyl thiolbenzoate, m.p. 140–141°.

Preparation of N-*benzoyl*-N,S-*diacetyl*-o-*aminothiophenol*

A solution of *o*-acetamidophenyl thiolacetate (0·96 g) and benzoyl chloride (1·0 g) in dry benzene (25 ml) containing anhydrous K_2CO_3 (3 g) was stirred at 20° for 3 days. The filtered solution yielded *triacyl compound*, m.p. 79–80° from light petroleum–benzene. (Found: C, 65·7; H, 4·9; S, 10·5. $C_{17}H_{15}NO_3S$ requires: C, 65·2; H, 4·8; S, 10·2%). The I.R. spectrum contained three bands in the carbonyl region.

Attempts to acylate N,S-dibenzoyl-*o*-aminothiophenol were not successful.

Preparation of benzothiazoles

2-*Phenylbenzothiazole.* Dissolution of *o*-benzamidothiophenol (1·0 g) in ethanol and removal of the solvent left 2-phenylbenzothiazole (0·9 g, 98%), m.p. 114°. Other benzothiazoles were obtained similarly.

Hydrolysis of N,S-*diacyl*-o-*aminothiophenols*

(i) *Analysis.* A solution of *o*-acetamidophenyl thiolbenzoate (0·518 g) in N alcoholic KOH (4 ml) was poured onto cold N H_2SO_4 aq (5 ml.). The precipitated thiol (0·4 g) was collected and washed with warm water. The filtrate and washings were combined, neutralized and evaporated to dryness. Chromatography of the residue on paper using propanol–ammonium carbonate indicated the presence of acetic (R_F 0·49) and benzoic (R_F 0·73) acids.

The mixture of benzothiazoles obtained from the crude thiol was examined by thin-layer chromatography using Kieselgel G (Stahl) with 50% ether–light petroleum: no components other than 2-methyl- and 2-phenyl-benzothiazole were detected. The mixture was analysed by comparison of the U.V. spectrum with those of synthetic mixtures and by gas-liquid chromatography on a silicone oil column at 100°. (Other mixtures were also analysed by comparison of the infrared spectra of solutions in carbon disulphide.)

(ii) *Kinetic studies.* The reactions were followed spectrophotometrically using ethanolic solutions (initial concentration 10^{-4} molar).

I.R. spectra were measured with a Perkin-Elmer model 21 spectrometer; U.V. spectra were measured with a Cary 14 spectrometer.

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