

811. *Thiadiazoles. Part XII.* The Ultraviolet Absorption Spectra of Some 1,2,4-Thiadiazoles.*

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The light-absorption properties, in the near-ultraviolet region, of several series of 1,2,4-thiadiazoles and their acyl derivatives are described, and are discussed with a view to establishing structural correlations.

Spectra are also given of amidinothioureas, thiobiurets, and dithiobiurets, which yield the above 1,2,4-thiadiazoles on oxidative cyclisation.

INFORMATION concerning the absorption spectra of certain 1,2,4-thiadiazoles has only recently become available. The studies of Goerdeler and his co-workers¹ have helped in deciding structural questions in this field,^{1,2} and in calculating ionisation constants in a number of cases.^{1c} In the present paper we record and discuss the light absorption properties, in the near-ultraviolet region, of variously substituted 1,2,4-thiadiazoles, and their reduced open-chain precursors incorporating the amidinothiono-system, chief amongst which figure amidinothioureas, thiobiurets, and dithiobiurets. Spectroscopic results are presented in Tables A—J and are discussed in that order. The synthesis of the compounds concerned has been described in Parts I—VII of this series.³

Amidinothioureas (see Table A and Fig. 1).—The spectrum of amidinothiourea (I; R = R' = R'' = H) shows two high-intensity maxima, at 240 and 273 m μ (Fig. 1). It appears that electronic interaction of the thiono- and the imino-group in this compound is chiefly responsible for its spectrum, since guanidine absorbs hardly at all,⁴ thiourea

* Part XI, *J.*, 1961, 1617.

¹ Goerdeler *et al.*, *Chem. Ber.*, (a) 1954, **87**, 57, 68; (b) 1955, **88**, 843, 1071; (c) 1956, **89**, 1033, 1534; (d) 1958, **91**, 1025; (e) 1960, **93**, 963.

² Scott, *Chem. and Ind.*, 1958, 463.

³ Kurzer *et al.*, *J.*, (a) 1955, 1, 2288; (b) 1956, 2345; (c) 1956, 4524; (d) 1957, 2999; (e) 1958, 379; 1959, 1064.

⁴ McFarlane, *Biochem. J.*, 1936, **30**, 1199.

Absorption spectra: λ (in $m\mu$), followed by $\log \epsilon$.

No.	R	R	Maximum	Minimum	Principal max.	Minimum	Maximum	Inflexion
A. <i>Amidinothioureas</i> , R·NH·CS·NH·C(:NH)·NHR'.								
1	H	H ^a	240	255	273	3-73	4-11	
2	Ph	H	240	243	279	3-56	4-40	300
3	<i>p</i> -C ₆ H ₄ Me	H	244	244	279	3-62	4-40	300
4	<i>p</i> -C ₆ H ₄ Br	H	248	248	282	3-64	4-45	300
5	Ph	Me	244	244	282	3-59	4-43	295
6	Ph	Me ₂ ^b	243	243	285	3-63	4-43	
7	Ph	Ph	253	253	298	3-91	4-44	
8	Me	Ph ^c	224	242s	260s	4-04	4-12	
9	H	<i>p</i> -C ₆ H ₄ Me·SO ₂ ^d	236	252	274	3-85	4-27	
10	Ph	<i>p</i> -C ₆ H ₄ Me·SO ₂	225s	243	261	4-18	4-37	
11	Ph	<i>p</i> -C ₆ H ₄ Me·SO ₂ ^e	219	219	248	4-13	282s	295s
s = Shallow maximum or minimum. ^a Also λ_{min} , 225 (3-87). ^b Compound Ph·NH·CS·NH·C(:NH)·NMe ₂ . ^c Hydrochloride. ^d Also λ_{min} , 228 (4-11). • Amidinoarea derivative.								
B. <i>Thioiurets</i> , R·NH·CS·NH·C(:NH)·OR'.								
12	H	H	229	232	255	3-21	4-19	
13	Me	H	232	232	256	3-32	4-20	
	Me	H ^f	232	232	250	3-72	4-17	
14	Me	Me ^e	229	229	250	3-86	4-13	260
15	Me	Et	226	226	250	3-97	4-53	270
16	Ph	H	228	228	245	4-09	4-23	
17	Ph	Me	242	242	274	3-66	4-26	287s
18	Ph	Et	241	241	275	3-66	4-25	305s
f In 0-0001N-HCl.								
C. <i>Dithioiurets</i> , R·NH·CS·NH·C(:NH)·SR'.								
19	H	H ^g	225	240	280	3-79	4-15	
20	Me	Me ^e	227	227	265s	3-80	4-17	
21	Pr ⁿ	Me ^e	234	234	267s	3-87	4-24	
22	Me	CH ₂ Ph	234	234	271	3-91	4-23	
23	Pr ⁿ	CH ₂ Ph ^e	264	264	292	3-92	4-31	
24	Ph	H ^h	248	252	296	3-77	4-34	
25	Ph	Me	254	254	297	3-84	4-36	
26	Ph	CH ₂ Ph	254	254	300	3-96	4-31	230
27	Ph	Ph	254	254	300	3-96	4-31	4-14
g See ref. 13. ^h Also λ_{min} , 234 (4-07).								

TABLE. (Continued.)

D. 3,5-Diamino-1,2,4-thiadiazole and its homologues (IV).

No.	R	R'	Maximum	Minimum	Principal max.	Minimum	Maximum	Inflection
28	H	H ⁱ			229	268	288	295
29	NH ₂	H ^j			247	279s	293	295
30	NH ₂	NH ₂	234	3-31	256	288	293	295
31	NHMe	NH ₂	237	3-45	257	279s	293	295
32	NHEt	NH ₂	238	3-45	258	260	273	295
33	NHPr ^a	NH ₂	238	3-46	258	260	273	295
34	NHPh	NH ₂ ^k	243	3-84	288	268	288	295
35	<i>p</i> -Me-C ₆ H ₄ -NH	NH ₂ ^l	243	3-86	288	268	288	295
36	<i>p</i> -Br-C ₆ H ₄ -NH	NH ₂ ^m	248	3-91	295	268	288	295
37	NHPh	NHMe	224	3-88	251	268	288	295
38	NHPh	NMe ₂	226	3-88	258	268	288	295
39	NHMe	NHPh	219	3-89	246	268	288	295
40	NHPh	NHPh	232	3-77	270	268	288	295
41	<i>p</i> -Me-C ₆ H ₄ -NH	<i>p</i> -Me-C ₆ H ₄ -NH	232	3-85	273	268	288	295

ⁱ In hexane; Goerdeler and Tegtmeyer, *Angew. Chem.*, 1955, 67, 302, and ref. l.c. ^j In H₂O (ref. 1a). ^k Also λ_{min.} 223 (3-93).

^m Also λ_{min.} 224 (3-83).

E. 3,5-Diamino-1,2,4-thiadiazole: acyl derivatives.

Deriv.

42	Diacetyl		225	4-43	225	279	296s	255-265 ⁿ
43	Dipropionyl		225	4-44	225	285	309	255-264 ⁿ
44	5-Amino-3-benzamido		237	4-01	256	279	296s	3-56
45	5-Amino-3- <i>p</i> -chlorobenzamido		238	4-02	257	285	309	3-57
46	5-Amino-3- <i>p</i> -nitrobenzamido		236	3-88	270	303s	332s	
47	Dibenzoyl		242	4-49	242	303s	332s	270
48	5-Amino-3-tosyl		227	4-20	227	270	296s	250
49	5-Amino-3- <i>m</i> -NO ₂ -C ₆ H ₄ -SO ₂		235	4-06	253	270	296s	270

ⁿ Plateau.

F. 3-Amino-5-methylamino-1,2,4-thiadiazole: acyl derivatives.

50	Monoacetyl	228	4-10	254	3-07	284	3-50	270
51	Monobenzoyl					238	4-41	265
52	Dibenzoyl					240	4-45	270
53	Tribenzoyl					237	4-52	250
54	Tosyl	218	4-33			229	4-22	262-266 ⁿ
55	Ditosyl					234	4-40	3-85
56	Tritosyl					234	4-62	3-85

G. 3-Amino-5-anilino-1,2,4-thiadiazole: acyl derivatives.

57	Diacetyl		227	4-43	227	293	3-82	255-265 ⁿ
58	Triacetyl		254	3-85	254	293	3-82	255-265 ⁿ
59	Monobenzoyl	244s	3-81	3-85	254	293	3-82	255-265 ⁿ
60	Tribenzoyl	225s	4-15	4-36	255	293	3-82	255-265 ⁿ
61	Tosyl ^o	221	4-43	4-55	255	293	3-82	255-265 ⁿ
62	<i>m</i> -NO ₂ -C ₆ H ₄ -SO ₂	226	4-30	4-24	288	293	3-82	255-265 ⁿ
63	Ditosyl	248s	4-15	283s	260	293	3-82	255-265 ⁿ
64	Tritosyl	228	4-26	4-64	235	293	3-82	255-265 ⁿ

^o Also λ_{min.} 215 (4-26).

TABLE. (Continued.)

H. 5-Alkyl(or aryl)amino-3-hydroxy(or mercapto)-1,2,4-thiadiazoles (IV).		3-Subst. R'		Maximum	Minimum	Principal max.	Minimum	Maximum	Inflexion
5-Subst. R in 5-NHR									
65	Me	OMe		218	225	247	226	218	255
66	Me	OEt		217s	226	247	227	217s	230
67	Me	SMe		219	227	235	227	219	260
68	Me	S-CH ₂ Ph		217s	228	236	228	217s	255
69	Pr ⁿ	SMe		217s	228	236	228	217s	230
70	Pr ⁿ	S-CH ₂ Ph		217s	228	236	228	217s	260
71	Ph	OH ^p		250s	259s	280	259s	250s	255
72	<i>p</i> -C ₆ H ₄ Me	OH ^q		251s	258s	281	258s	251s	230
73	Ph	OMe		251s	243	282	243	251s	260
74	Ph	OEt		252	244	283	244	252	230
75	Ph	SMe ^r		255	267	287s	267	255	230
76	Ph	S-CH ₂ Ph ^r		255	271	288	271	255	260
77	Ph	SPh		245	229	275s	229	245	230
78	Ph	SOMe ^t		245	263	297	263	245	230
79	Ph	SO ₂ Me ^u		245	263	300	263	245	260

^p Also λ_{min.} 228 (3.81). ^q Also λ_{min.} 230 (3.85). ^r Also λ_{min.} 225 (3.95). ^s Also λ_{min.} 229 (4.08). ^t Also λ_{min.} 231 (3.91). ^u Also λ_{min.} 234 (3.80).

I. Acyl derivatives of 5-amino-3-hydroxy(or alkoxy or alkylthio)-1,2,4-thiadiazoles (IV; R = NHPh).		Deriv.		Maximum	Minimum	Principal max.	Minimum	Maximum	Inflexion
R'	R								
80	OH	Diacetyl		231	231	252s	231	231	260—275
81	OH	Dibenzoyl		222	246	228	222	222	290
82	OH	Monotosyl		222	246	286	222	222	265—275
83	OMe	Monoaetyl		222	243	265	222	222	4.08 ⁿ
84	OMe	Monobenzoyl		228s	256	281	228s	228s	4.03 ⁿ
85	SMe	Monoaetyl		237	237	237	237	237	
86	SMe	Monobenzoyl		231s	231s	247	231s	231s	

J. 3-Substituted 5-aryl-1,2,4-thiadiazoles (IV).		R'		Maximum	Minimum	Principal max.	Minimum	Maximum	Inflexion
R	R'								
87	Ph	NH ₂ ^v		230	3.92	252	230	230	287—300
88	Ph	NH ₂ ^w		224	4.17	244s	224	224	3.71 ⁿ
89	Ph	NH ₂ ^x		224	4.29	247	224	224	287—300
90	Ph	NH ₂ ^z		238s	4.18	252	238s	238s	3.78
91	<i>p</i> -C ₆ H ₄ Cl	NH ₂		220s	4.01	235s	220s	220s	3.79
92	<i>p</i> -C ₆ H ₄ NO ₂	NH ₂		235	3.73	274	235	235	3.82
93	Ph	OH		227	3.75	248	227	227	260
	Ph	OH ^y		230	3.70	260	230	230	260
	Ph	OH ^z		230	3.70	260	230	230	260

^v Monoaetyl derivative. ^w Dibenzoyl derivative. ^x Monotoluene-*p*-sulphonyl derivative. ^y In 0.1N-aq. NaOH. ^z In 2N-aq. HCl. * Increasing absorption beyond 283 mμ.

shows only one maximum (at 240 $m\mu$),⁵ and biguanide also exhibits only one peak⁶ (at 230 $m\mu$, $\log \epsilon$ 4, in aqueous solution buffered at pH 9).

Marked changes in the absorption are caused by the introduction of substituents into amidinothiourea: greater effects are produced by *N*-aryl substituents in the thioureidothan in the amidino-group (see Table A), possibly because the thiono- is a more powerful chromophore than the amido-group.⁷ Thus, *N*-amidino-*N'*-arylthioureas (I; R = Ar, R' = R'' = H) (all having identical spectra, apart from the expected⁸ small bathochromic shifts; see Fig. 1) give rise to one broad peak (275–280 $m\mu$) and a point of inflexion, presumably a partly obscured *B* band.⁷ The additional introduction of alkyl groups into these structures is virtually without effect, the spectra (5, 6) of *N*-methyl- (I; R = Ph, R' = Me, R'' = H) and *NN*-dimethyl-amidino-*N'*-phenylthiourea (I; R = Ph, R' = R'' = Me) resembling that (2) of the parent (I; R = Ph, R' = R'' = H). Also, the absorption curve due to *N*-phenyl-*N'*-phenylamidinothiourea (I; R = R' = Ph, R'' = H)

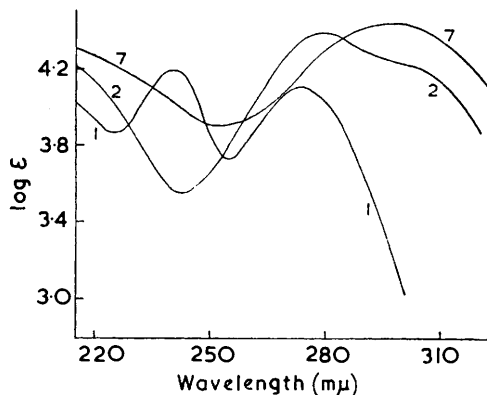


FIG. 1. Spectra of: amidinothiourea (1); *N*-amidino-*N'*-phenylthiourea (2); *N*-phenyl-*N'*-phenylamidinothiourea (7).

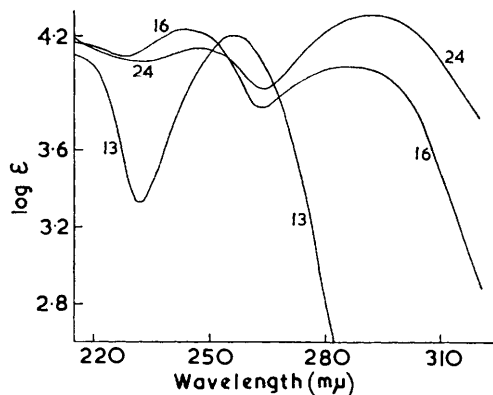


FIG. 2. Spectra of: 1-methyl-2-thiobiuret (13); 1-phenyl-2-thiobiuret (16); 1-phenyl-dithiobiuret (24).

(Fig. 1) shows a greater similarity to that (2) of *N*-amidino-*N'*-phenylthiourea (I; R = Ph, R' = R'' = H) than to that (8) of *N*-methyl-*N'*-phenylamidinothiourea (I; R = Me, R' = Ph, R'' = H). The resemblance of the spectra of amidinothiourea and *N*-toluene-*p*-sulphonamidinothiourea indicates that the tosyl group has little effect in this environment, the sulphonyl group preventing interaction between the aromatic and the amidino-group (compare spectra 1 and 9).

The importance of the contribution of the sulphur atom to the spectra of amidinothioureas is emphasised by a comparison of those of *N*-phenyl-*N'*-toluene-*p*-sulphonamidino-thiourea (I; R = Ph, R' = H, R'' = *p*-Me·C₆H₄·SO₂) and -urea: there are no obvious common features (see spectra 10 and 11), but the thiourea shows the expected^{7,9,10} additional absorption bands at the longer wavelengths. The ability of sulphur to expand its outermost shell of electrons to a decet and its consequent power, in contrast to oxygen, to accept electrons account for the greater complexity of the spectra of compounds derived from thiourea.^{10,11}

⁵ Grammaticakis, *Bull. Soc. chim. France*, 1953, 86.

⁶ Hirt and Schmitt, *Spectrochim. Acta*, 1958, 12, 127.

⁷ Gillam and Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Arnold, London, 1957.

⁸ Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," Wiley, New York and London, 1951.

⁹ Clow and Helmrich, *Trans. Faraday Soc.*, 1940, 36, 685.

¹⁰ Fehnel and Carmack, *J. Amer. Chem. Soc.*, 1949, 71, (a) 84, (b) 2889.

¹¹ Passerini, in Kharasch (ed.), "Organic Sulfur Compounds," Pergamon Press, Oxford, 1961, Vol. I, pp. 57, 64.

Thiobiurets (see Table B and Fig. 2).—Thiobiuret shows the single absorption maximum of thiourea⁵ displaced towards the longer wavelengths (by 15 m μ , to 255 m μ) and of increased intensity (to log ϵ 4.19). The presence of a phenyl group in the thiourea portion (II; R = Ph, R' = R'' = H) produces a second wide maximum (at 280—295 m μ) (Fig. 2). The higher intensity and bathochromic displacement of this benzenoid B band, compared with the main maximum of benzene itself, and the absence of fine structure are ascribed to the effect of the unshared electron pair of the adjacent nitrogen on the resonance of the aromatic ring. *N*-Alkylation hardly affects the spectrum of thiobiuret (see spectra 12, 13), but *O*-alkylation, resulting in the thioisobiuret structure (IIa; R = Ph, R' = Me or Et, R'' = H), causes a pronounced general widening (spectra 14, 15) or shift (spectra 17, 18) of the band towards the longer wavelengths. These differences in the spectra of thiobiurets

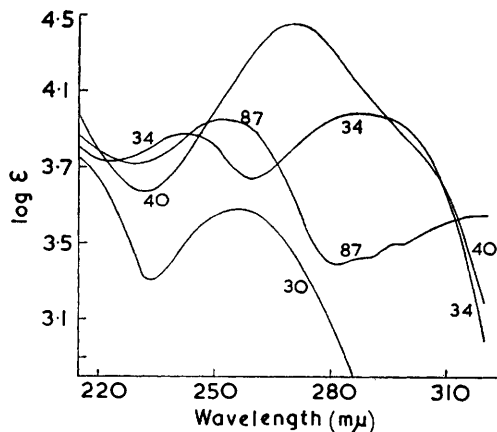
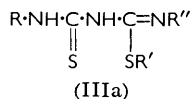
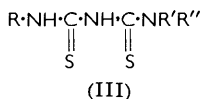
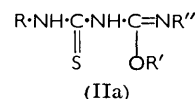
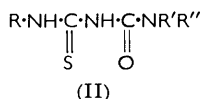
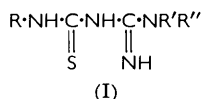


FIG. 3. Spectra of: 3,5-diamino- (30), 3-amino-5-anilino- (34), 3,5-dianilino- (40), and 3-amino-5-phenyl-1,2,4-thiadiazole (87).

(II) and their *O*-alkyl homologues (IIa) suggest that, in ethanol, the former exist predominantly in the keto-form. The application of ultraviolet-absorption measurements in demonstrating the isomerisation of 1,*O*-dimethyl- to 1,*S*-dimethyl-2-thioisobiuret has already been described.¹²



Dithiobiurets (see Table C).—Dithiobiuret gives rise to two peaks, at 225 and 280 m μ .¹³ The spectra (20—23) of several 1-alkyl-*S*⁴-aralkyliso-2,4-dithiobiurets (hydrochlorides, IIIa) are characterised by a wide intense band in the 270 m μ region, and are modified and displaced towards the longer wavelengths in the spectra of the 1-aryl homologues (25—27). The nature of the *S*⁴-substituent (IIIa, R') exerts less influence, suggesting that the thioenolic character of the molecule is the dominating factor determining the spectra of these compounds. 1-Phenyldithiobiuret (III; R = Ph, R' = R'' = H) having a spectrum (24, Fig. 2) distinct from those of the 1-aryl-*S*⁴-iso-2,4-dithiobiurets (IIIa) may therefore be considered to exist in the thiono-form in ethanolic solution. This argument is not invalidated by comparing hydrochlorides and bases, since salt-formation results in only insignificant hypsochromic shifts in this series (see, for example, spectra, 13 and 20—23).

3,5-Diamino-1,2,4-thiadiazole and its Homologues (see Table D and Fig. 3).—As in

¹² Kurzer and Taylor, *J.*, 1960, 470.

¹³ American Cyanamid Co., "New Products Bulletin," Coll. Vol. I, 1952, p. 54.

benzene,¹⁴ the introduction of amino-groups into the heteroaromatic 1,2,4-thiadiazole nucleus displaces the absorption maximum strongly towards the longer wavelengths. Thus, the peak due to the parent compound (IV; R = R' = H)^{1a} is moved from 229 to 247 m μ in 5-amino-^{1a} and to 256 m μ in 3,5-diamino-1,2,4-thiadiazole (spectra 28—30). Alkylation of the 5-amino-group produces merely the expected further very small bathochromic and hyperchromic displacements (spectra 31—33), but arylation introduces a second more intense maximum at *ca.* 290 m μ (spectra 34—36). This, it is suggested, is a *K*-band due to conjugation between the aromatic and the heteroaromatic component, obscuring the benzenoid absorption band. The maximum at 245 m μ of lower intensity is probably the *E* band⁷ of the aromatic portion, displaced into this region owing to its particular structural environment. The peak in the 290 m μ zone recurs in most 5-aryl-amino-1,2,4-thiadiazoles (cf. spectra 34—38, 71—76) and may thus be regarded as indicative of this structure.

Conclusions regarding the contribution of tautomers to the spectra of the diamino-thiadiazoles (IV; R = R' = NH₂, etc.) are not possible at present because suitable ring-alkylated compounds were not available for comparison. The similarity of the spectra of 3-amino-5-anilino-1,2,4-thiadiazole (34) and its 3-methylamino- (37) and 3-dimethylamino-homologues (38) suggests that the parent compound (IV; R = NHPH, R' = NH₂) exists in the 3-amino-form. The same conclusions have been reached concerning the 5-amino-group in 1,2,4-thiadiazoles from both spectrographic^{1a} and polarographic¹⁵ evidence. The methylation causes bathochromic displacement and exaltation of the shorter-wavelength band. A similar general trend is observed in the spectra of aniline or 2-aminopyridine and their *N*-mono- and *N*-di-methyl derivatives.¹⁶

Acyl Derivatives of 3,5-Diamino-1,2,4-thiadiazole and its Homologues (see Tables E—G).—The structures assigned to acylated 1,2,4-thiadiazoles obtained by direct acylation are mostly unconfirmed; in a very few cases additional degradative or synthetic evidence^{3c,d} is available (see Table E, compounds 44—46, 48, 49, 61). An attempt has now been made to employ spectrographic evidence in elucidating further some of these structures.

(i) *Acetyl derivatives.* On acetylation, 3,5-diamino-1,2,4-thiadiazole yields a diacetyl derivative to which structure (IV; R = R' = NHAc) has been assigned;^{3a} this is strongly supported, though not completely established, by its synthesis by the oxidation of acetylthiourea.¹⁷ Its spectrum (42) features an intense maximum at 225 and a plateau at 255—265 m μ . The diacetyl derivative of 3-amino-5-anilino-1,2,4-thiadiazole shows an almost identical spectrum (57) and is therefore assigned structure (V; R = Me, R' = Ph). The difference in the spectra of the diacetyl derivative (57) and the parent (34), in particular the loss of the peak at 288 m μ (in 57), may be the result of the absence of resonance contributions by structures of types (VI) and (VII). Provided that structure (V; R = Me, R' = Ph) for the diacetyl derivative is correct, it is suggested that the corresponding triacetyl derivative should be represented as (VIII; R = Me, R' = Ph) rather than (IX; R = Me, R' = Ph) as originally postulated.^{3b} The formulation of the monoacetyl derivative of 3-amino-5-methylamino-1,2,4-thiadiazole as the 3-acetamido-compound, previously proposed on chemical grounds,^{3a} is admissible on the basis of its absorption spectrum (50).

(ii) *Benzoyl derivatives.* The general outline of the spectrum (44) of 5-amino-3-benzamido-1,2,4-thiadiazole, the structure of which is established with reasonable certainty* by its synthesis,^{3c} is similar to that (50) of the 3-acetamido-5-methylamino-analogue,

* The possibility of the alternative formulation of the compounds as 2-benzoyl(tosyl)-3,5-di-imino-1,2,4-thiadiazolidines has not been completely eliminated.

¹⁴ Braude, *Ann. Reports*, 1945, **42**, 105.

¹⁵ Sturm and Hans, *Angew. Chem.*, 1955, **67**, 743.

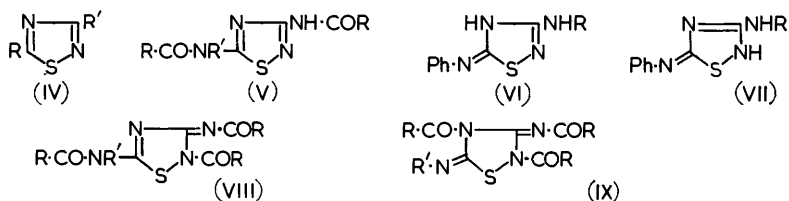
¹⁶ Ley and Specker, *Ber.*, 1939, **72**, 192; Anderson and Seegar, *J. Amer. Chem. Soc.*, 1949, **71**, 340.

¹⁷ Walter, *Angew. Chem.*, 1958, **70**, 371.

though considerably displaced towards the longer wavelengths. The presence of a *p*-chloro- or *p*-nitro-group in the benzoyl radical produces the usual bathochromic shifts, small in the former case, but sufficiently large in the latter to bring part of the spectral envelope into the visible region.^{7,8}

Since the spectrum of monobenzoyl-3-amino-5-methylamino-1,2,4-thiadiazole (51) is quite distinct from that of 5-amino-3-benzamido-1,2,4-thiadiazole (44), it is unlikely that the originally postulated^{3a} 3-benzamido-structure can be assigned to this compound; of the possible formulations, the 5-benzamido-structure (IV; R = NMeBz, R' = NH₂) may provisionally be suggested (see also below).

The introduction of a second and a third benzoyl group is attended by profound changes in the absorption curves. The spectra of the dibenzoyl derivative of 3,5-diamino- and the di- and the tri-benzoyl derivative of 3-amino-5-methylamino-1,2,4-thiadiazole are remarkably similar (spectra 47, 52, 53). If we assume the 3,5-dibenzamido-structure (IV; R = R' = NHBz) for the first compound by analogy with the 3,5-diacetamido-derivative,^{3a,17} the last two may be represented as (V) and (VIII) (R' = Me, R = Ph), respectively. The similarity of the spectrum (60) of the tribenzoyl derivative of the 5-anilino-homologue permits the same interpretation, leading to its formulation as (VIII; R = R' = Ph) rather than (IX; R = R' = Ph) previously postulated.^{3b}



(iii) *Sulphonyl derivatives.* 5-Amino-3-toluene-*p*-sulphonamido-1,2,4-thiadiazole, the structure * of which is supported by synthesis,^{3d} and the corresponding 5-methylamino-homologue have similar spectra (48 and 54); the latter may therefore be represented as (IV; R = NHMe, R' = *p*-Me·C₆H₄·SO₂·NH) as previously suggested.^{3b,d} A noteworthy feature of the spectra of the mono-, di-, and tri-tosyl derivatives of 3-amino-5-methylamino-1,2,4-thiadiazole (54—56) is the regular hyperchromic displacement of the maximum by about 0.2 unit (on the log ϵ scale) for each additional tosyl group, while the position of the peak is substantially unaffected. There appears to be very little conjugation between the heterocyclic ring and these substituents.

In contrast, the spectra of the mono-, di-, and tri-tosyl derivatives (61, 63, 64) of 3-amino-5-anilino-1,2,4-thiadiazole differ markedly from one another, presumably as a result of the influence of the anilino-group. The spectrum (61) of the monotosyl derivative, known from other evidence^{3d} to be very probably 5-anilino-3-toluene-*p*-sulphonamido-1,2,4-thiadiazole, resembles in outline that (34) of the parent compound (IV; R = NPh, R' = NH₂). As expected, the tosyl group has little effect on the conjugation of the main chromophore.

3-Hydroxy(and Mercapto)-5-amino-1,2,4-thiadiazole and its Homologues (see Tables H, I).—The spectra (65, 66) of 3-alkoxy-5-methylamino-1,2,4-thiadiazoles are almost identical with that (31) of 3-amino-5-methylamino-1,2,4-thiadiazole, except for the required^{14,18} hypsochromic displacement (by 10 m μ). This may be taken as additional support in favour of the 3-amino-configuration of the latter compound. The 3-alkylthio-1,2,4-thiadiazoles differ in their spectra (67—70) from the alkoxy-series in a manner comparable with that of 2-methylthio- and 2-methoxy-4-methylpyrimidine in neutral solution.¹⁹ The maxima in the 3-mercapto-1,2,4-thiadiazole series are, however, shallow, and

* See footnote, p. 4197.

¹⁸ Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127; Morton and Stubbs, *J.*, 1940, 1347.

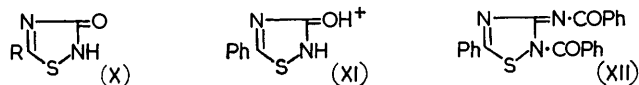
¹⁹ Marshall and Walker, *J.*, 1951, 1004.

for 5-alkylamino-3-benzylthio-1,2,4-thiadiazoles (68, 70) are reduced to points of inflexion.

The spectrum (71) of 5-anilino-3-hydroxy-1,2,4-thiadiazole bears a close resemblance to that (34) of the 3-amino-analogue for which the 3-amino-configuration seems most likely (see above). In spite of this, the differences in the spectra of 5-anilino-3-hydroxy- and 3-alkoxy-5-anilino-1,2,4-thiadiazoles (71, 73, 74) suggest that ketonic tautomers, such as (X; R = NPh), of the hydroxy-compound must contribute to the resultant absorption curve. Thus, the 5-alkoxy-homologues (73, 74), which must have the enolic configuration, lack the band at 250 $m\mu$ present in the spectrum (71) of the parent. 4-Methylpyrimid-2-one and 2-methoxy-4-methylpyrimidine are comparable:¹⁹ in neutral solution, the former exhibits maxima at 213 and 296 $m\mu$, which are replaced by a single peak (at 264 $m\mu$) in the latter.

3-Alkylthio-5-anilino-1,2,4-thiadiazoles exhibit twin peaks (75, 76) which give way, in the 3-phenylthio-compound, to a single broad band (77) in the region of 275 $m\mu$. It appears that there is considerable electronic interaction between the phenyl group, sulphur, and the heterocyclic ring. The existence of such conjugation between benzene rings and an adjacent sulphide function has been deduced from studies of the spectra of diphenyl sulphide and methyl phenyl sulphide.^{10a, 11}

Conversion of 5-anilino-3-methylthio-1,2,4-thiadiazole into the sulphoxide and then the sulphone causes a progressive separation and lowering of the resulting absorption maxima (spectra 75, 78, 79). A similar hypochromic effect occurs with methyl phenyl sulphide and sulphone,^{10b} and, as in the 1,2,4-thiadiazole series, no characteristic absorption bands attributable to the sulphone function are observed.



3-Substituted 5-Phenyl-1,2,4-thiadiazoles (see Table J).—The spectrum of 3-hydroxy-5-phenyl-1,2,4-thiadiazole in neutral solution (93) differs from that of 3-amino-5-phenyl- (87, Fig. 3) but resembles that of 5-anilino-3-hydroxy-1,2,4-thiadiazole (71). By the arguments given above, it is therefore likely that the ketonic tautomer (X; R = Ph) contributes substantially to the spectrum. This view is supported by the fact that the absorption curve of 3-hydroxy-5-phenyl-1,2,4-thiadiazole in alkaline solution, where the anion is bound to predominate, is coincident with that (87) of the 3-amino-analogue. It also follows that, in neutral solution, the latter, like most comparable amino-compounds of this series, exists in the amino- rather than the imino-form. The identity of spectra of anions of phenols and of amines in the aromatic and heterocyclic field is well authenticated.²⁰

The spectrum (89) of the dibenzoyl derivative of 3-amino-5-phenyl-1,2,4-thiadiazole in ethanol resembles in outline that (93) of 3-hydroxy-5-phenyl-1,2,4-thiadiazole in 2*N*-sulphuric acid, except for the hyperchromic displacement. Since in acid solution, form (XI) is likely to make a significant contribution to the spectrum of the hydroxy-compound, this observation supports the proposed^{3c} structure (XII) for the above dibenzoyl derivative.

EXPERIMENTAL

Ultraviolet absorption spectra were determined between 210 and 320 $m\mu$ with a Unicam S.P. 500 spectrophotometer, incorporating 10 mm. silica cells. The solvent was "AnalaR" ethanol, and the concentrations ranged near 10⁻⁴M.

The compounds were synthesised as described in Parts I—VII of this series.³ Thiobiuret was obtained in 20—25% overall yield by Hecht's and Wunderlich's method.²¹

²⁰ Albert, *Quart. Rev.*, 1952, **6**, 197.

²¹ Wunderlich, *Ber.*, 1886, **19**, 449; Hecht, *Ber.*, 1892, **25**, 749.

1-(*NN*-Dimethylamidino)-3-phenylthiourea.—To the suspension obtained on adding sodium (0.5 g., 0.022 g.-atom) to anhydrous acetone (25 ml.), *NN*-dimethylguanidine sulphate (3.40 g., 0.025 mole) was added. The stirred suspension was refluxed during 15 min. and then treated dropwise with phenyl isothiocyanate (2.35 g., 0.0175 mole). Refluxing was continued for 15 min., most of the solvent removed by distillation, and the residual suspension stirred into water (150 ml.). The granular precipitate, on crystallisation from ethanol, formed needles (2.72 g., 70%) of the *thiourea*, m. p. 161—163° (decomp.) (Found: C, 54.4; H, 6.1. $C_{10}H_{14}N_4S$ requires C, 54.05; H, 6.3%).

5-Anilino-3-dimethylamino-1,2,4-thiadiazole.—A boiling solution of the foregoing thiourea (1.11 g., 0.005 mole) in ethanol (10 ml.) was treated with 6% hydrogen peroxide (8.5 ml., 0.015 mole) and concentrated hydrochloric acid (0.5 ml., 0.005 mole), and boiling continued during 3 min. Addition of the solution to water (60 ml.) gave a crystalline precipitate which consisted, after crystallisation from a large volume of ethanol, of prismatic needles (0.77 g., 60%) of the *thiadiazole hydrochloride*, m. p. 229—231° (decomp.) (Found: C, 47.2; H, 4.8; N, 21.7. $C_{10}H_{12}N_4S.HCl$ requires C, 46.8; H, 5.1; N, 21.8%).

Alternatively, addition of the oxidised solution to 2*N*-ammonia (75 ml.) gave a white precipitate, which consisted, after crystallisation from ethanol-light petroleum (b. p. 60—80°), of lustrous prisms of the *base*, m. p. 168—169° (0.82 g., 75%) (Found: C, 54.2; H, 5.3; N, 25.6. $C_{10}H_{12}N_4S$ requires C, 54.5; H, 5.45; N, 25.45%).

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