423. *Potential Antiviral Thiourea Derivatives.*

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Numerous thiourea derivatives, including 4-aryl-, 1 : 4- and 2 : 4-diaryl-, 1-(arylaminothioformyl)-, 4-aryl-1-(arylaminothioformyl)-thiosemicarbazides, and aryliminothiazolines, have been synthesised as potential antiviral agents.

Preliminary chemotherapeutic tests on mice showed recently that a number of thiourea derivatives are effective against infection by influenza virus (strain PR 8, type A).[1] A broad investigation has been made of the relation between chemical structure and antiviral activity in sulphur derivatives bearing a thiourea or a thiosemicarbazide group, and the present paper records the chemical work.

Several compounds showing antiviral properties contain an $\rangle N{\cdot}N\langle$ group, as is the case with some thiosemicarbazones [2] and *NN*-dimethylaminobenzaldehyde *iso*nicotinoylhydrazone; [1] this suggested the preparation of substances bearing both a sulphur atom and a hydrazine group. The reaction of aryl *iso*thiocyanates with hydrazine hydrate [3] in great excess and at low temperature in ethanol readily gave 4-arylthiosemicarbazides $Ar{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}NH_2$; under these conditions, only one amino-group of hydrazine reacted, and the products were purer than those obtained by hydrazinolysis of *NN'*-diarylthioureas.[4] Among the substances thus prepared, 4-*p*-fluorophenylthiosemicarbazide was remarkable for its high toxicity in animals. 4-Arylthiosemicarbazides with aryl *iso*thiocyanates gave

$Ar{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}NH{\cdot}CS{\cdot}NHAr'$ (I) $\qquad$ $Ar{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}NH{\cdot}CO{\cdot}NHAr'$ (II)

NN'-di(arylaminothioformyl)hydrazines (I) (Table 1); with aryl *iso*cyanates, the reaction was more violent but led to a parallel series (II) (Table 2).

[1] Buu-Hoï, Gley, Xuong, and Bouffanais, *Compt. rend.*, 1954, **238**, 2582.
[2] Minton, Officer, and Thompson, *J. Immunol.*, 1953, **70**, 222, 229.
[3] Cf. Pulvermacher, *Ber.*, 1893, **26**, 2812.
[4] Busch and Bauer, *Ber.*, 1900, **33**, 1061.

TABLE 1. 4-*Aryl*-1-(*arylaminothioformyl*)*thiosemicarbazides*.

	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
1-(*Anilinothioformyl*) *compounds*.						
4-*p*-C_6H_4F	221°	$C_{14}H_{13}N_4S_2F$	52·2	4·0	52·5	4·0
4-*p*-C_6H_4Cl	216	$C_{14}H_{13}N_4S_2Cl$	49·6	3·9	49·9	3·8
4-*p*-C_6H_4Br	219	$C_{14}H_{13}N_4S_2Br$	43·7	3·3	44·0	3·4
4-*p*-Tolyl	210	$C_{15}H_{16}N_4S_2$	56·9	4·8	56·9	5·0
4-(2 : 4-Xylyl)	205	$C_{16}H_{18}N_4S_2$	58·0	5·3	58·2	5·4
4-(2 : 3-Xylyl)	198	$C_{16}H_{18}N_4S_2$	58·3	5·4	58·2	5·4
4-*p*-C_6H_4·OMe	211	$C_{15}H_{16}ON_4S_2$	54·0	4·6	54·2	4·8
4-*o*-C_6H_4·OMe	172	$C_{15}H_{16}ON_4S_2$	54·3	4·5	54·2	4·8
4-*p*-C_6H_4·OEt	219	$C_{16}H_{18}ON_4S_2$	55·1	5·2	55·4	5·2
4-*o*-C_6H_4·OEt	159	$C_{16}H_{18}ON_4S_2$	55·2	5·0	55·4	5·2
4-*p*-C_6H_4·O·CH_2Bu^i	209	$C_{19}H_{24}ON_4S_2$	58·6	6·1	58·8	6·2
4-α-$C_{10}H_7$	191	$C_{18}H_{16}N_4S_2$	61·0	4·5	61·3	4·5
4-β-$C_{10}H_7$	201	$C_{18}H_{16}N_4S_2$	61·2	4·7	61·3	4·5
1-(p-*Fluoroanilinothioformyl*) *compounds*.						
4-*p*-C_6H_4F	230	$C_{14}H_{12}N_4S_2F_2$	49·5	3·4	49·7	3·6
4-*p*-C_6H_4Cl	234	$C_{14}H_{12}N_4S_2ClF$	47·1	3·2	47·4	3·4
4-*p*-C_6H_4Br	238	$C_{14}H_{12}N_4S_2BrF$	42·0	3·2	42·1	3·0
4-*p*-Tolyl-	231	$C_{15}H_{15}N_4S_2F$	54·1	4·5	53·9	4·5
4-*m*-Tolyl-	219	$C_{15}H_{15}N_4S_2F$	53·6	4·6	53·9	4·5
4-*p*-C_6H_4·OMe	229	$C_{15}H_{15}ON_4S_2F$	51·5	4·5	51·4	4·3
4-*p*-C_6H_4·OEt	229	$C_{16}H_{17}ON_4S_2F$	52·8	4·8	52·7	4·7
4-α-$C_{10}H_7$	206	$C_{18}H_{15}N_4S_2F$	58·1	4·3	58·4	4·1
4-β-$C_{10}H_7$	220	$C_{18}H_{15}N_4S_2F$	58·5	4·2	58·4	4·1
1-(p-*Chloroanilinothioformyl*) *compounds*.						
4-*p*-C_6H_4Cl	232	$C_{14}H_{12}N_4S_2Cl_2$	45·3	3·5	45·3	3·2
4-*p*-C_6H_4Br	234	$C_{14}H_{12}N_4S_2BrCl$	40·1	3·2	40·4	2·9
4-*p*-Tolyl-	235	$C_{15}H_{15}N_4S_2Cl$	51·0	4·2	51·3	4·3
4-*p*-C_6H_4·OMe	228	$C_{15}H_{15}ON_4S_2Cl$	49·0	4·2	49·1	4·1
4-*p*-C_6H_4·OEt	230	$C_{16}H_{17}ON_4S_2Cl$	50·7	4·3	50·5	4·5
4-α-$C_{10}H_7$	212	$C_{18}H_{15}N_4S_2Cl$	55·8	4·1	55·9	3·9
4-β-$C_{10}H_7$	221	$C_{18}H_{15}N_4S_2Cl$	55·6	4·0	55·9	3·9
1-(p-*Bromoanilinothioformyl*) *compounds*.						
4-*p*-C_6H_4Br [a]	234°	$C_{14}H_{12}N_4S_2Br_2$	36·3	2·9	36·5	2·6
4-*p*-Tolyl-	233	$C_{15}H_{15}N_4S_2Br$	45·5	3·6	45·6	3·8
4-*p*-C_6H_4·OMe	231	$C_{15}H_{15}ON_4S_2Br$	43·5	3·5	43·8	3·6
4-*p*-C_6H_4·OEt	228	$C_{16}H_{17}ON_4S_2Br$	45·0	4·2	45·2	4·0
4-α-$C_{10}H_7$	215	$C_{18}H_{15}N_4S_2Br$	50·2	3·7	50·1	3·7
4-β-$C_{10}H_7$	223	$C_{18}H_{15}N_4S_2Br$	49·9	3·6	50·1	3·7
1-(p-*Toluidinothioformyl*) *compounds*.						
4-*p*-Tolyl- [b]	227	$C_{16}H_{18}N_4S_2$	58·0	5·5	58·2	5·4
4-*p*-C_6H_4·OMe	225	$C_{16}H_{18}ON_4S_2$	55·3	5·2	55·5	5·2
4-*p*-C_6H_4·OEt	231	$C_{17}H_{20}ON_4S_2$	56·3	5·5	56·6	5·5
4-α-$C_{10}H_7$	204	$C_{19}H_{18}N_4S_2$	62·1	5·0	62·3	4·9
4-β-$C_{10}H_7$	219	$C_{19}H_{18}N_4S_2$	62·5	5·0	62·3	4·9
1-(p-*Anisidinothioformyl*) *compounds*.						
4-*p*-C_6H_4·OMe	237	$C_{16}H_{18}O_2N_4S_2$	52·7	5·1	53·0	4·9
4-*p*-C_6H_4·OEt	227	$C_{17}H_{20}O_2N_4S_2$	54·2	5·1	54·3	5·3
4-α-$C_{10}H_7$	204	$C_{19}H_{18}ON_4S_2$	59·3	4·6	59·6	4·7
4-β-$C_{10}H_7$	225	$C_{19}H_{18}ON_4S_2$	59·3	4·5	59·6	4·7
1-(p-*Phenetidinothioformyl*) *compounds*.						
4-*p*-C_6H_4·OEt	239	$C_{18}H_{22}O_2N_4S_2$	55·5	5·3	55·4	5·6
4-α-$C_{10}H_7$	202	$C_{20}H_{20}ON_4S_2$	60·8	5·3	50·6	5·0
4-β-$C_{10}H_7$	227	$C_{20}H_{20}ON_4S_2$	60·3	5·1	60·6	5·0

[a] Guha (*J. Amer. Chem. Soc.*, 1923, **45**, 1041) prepared this compound from 4-bromophenyl *iso*thiocyanate and hydrazine sulphate in the presence of sodium carbonate, and gave m. p. 213°. [b] Fromm[9] gave m. p. 205°.

TABLE 2. 4-*Aryl*-1-(*arylaminoformyl*)*thiosemicarbazides* (II).

1-Aryl	M. p.	Formula	Found: N (%)	Reqd.: N (%)
4-p-Fluorophenyl compounds.				
p-C_6H_4Cl	280°	$C_{14}H_{12}ON_4SClF$	16·6	16·5
p-C_6H_4Br	281	$C_{14}H_{12}ON_4SBrF$	14·3	14·6
p-C_6H_4·OEt	233	$C_{16}H_{17}O_2N_4SF$	15·7	16·0
4-m-Chlorophenyl compounds.				
p-C_6H_4Cl	226	$C_{14}H_{12}ON_4SCl_2$	15·5	15·7
p-C_6H_4Br	241	$C_{14}H_{12}ON_4SBrCl$	13·9	14·0
4-m-Tolyl compound.				
p-C_6H_4Br	248	$C_{15}H_{15}ON_4SBr$	14·6	14·7
4-p-Tolyl compounds.				
p-C_6H_4Cl	274	$C_{15}H_{15}ON_4SCl$	16·4	16·7
p-C_6H_4Br	288	$C_{15}H_{15}ON_4SBr$	14·8	14·7
p-C_6H_4·OEt	246	$C_{17}H_{20}O_2N_4S$	16·0	16·2
4-p-Chlorophenyl compounds.				
p-C_6H_4Cl	273	$C_{14}H_{12}ON_4SCl_2$	15·6	15·7
p-C_6H_4Br	279	$C_{14}H_{12}ON_4SBrCl$	13·7	14·0
p-C_6H_4·OEt	246	$C_{16}H_{17}O_2N_4SCl$	15·3	15·3
4-p-Bromophenyl compounds.				
p-C_6H_4Cl	277°	$C_{14}H_{12}ON_4SBrCl$	13·7	14·0
p-C_6H_4Br	283	$C_{14}H_{12}ON_4SBr_2$	12·5	12·6
p-C_6H_4·OEt	248	$C_{16}H_{17}O_2N_4SBr$	13·3	13·6
4-p-Methoxyphenyl compounds.				
p-C_6H_4Cl	268	$C_{15}H_{15}O_2N_4SCl$	15·8	15·9
p-C_6H_4Br	276	$C_{15}H_{15}O_2N_4SBr$	14·2	14·1
p-C_6H_4·OEt	237	$C_{17}H_{20}O_3N_4S$	15·2	15·5
4-p-Ethoxyphenyl compounds.				
p-C_6H_4Cl	272	$C_{16}H_{17}O_2N_4SCl$	15·2	15·3
p-C_6H_4Br	278	$C_{16}H_{17}O_2N_4SBr$	13·3	13·6
p-C_6H_4·OEt	246	$C_{18}H_{22}O_3N_4S$	15·0	14·9
4-p-Ethylphenyl compounds				
Ph	233	$C_{16}H_{18}ON_4S$	17·6	17·8
p-C_6H_4·OEt	252	$C_{18}H_{22}O_2N_4S$	15·5	15·6
4-β-Naphthyl compounds.				
p-C_6H_4Cl	262	$C_{18}H_{15}ON_4SCl$	15·0	15·1
p-C_6H_4Br	270	$C_{18}H_{15}ON_4SBr$	13·1	13·4
p-C_6H_4·OEt	249	$C_{20}H_{20}O_2N_2S$	14·6	14·7

TABLE 3. *Thiosemicarbazides* (III) *and* (IV).

4-Aryl	M. p.	Formula	Found (%): C	H	Reqd. (%): C	H
2-Phenyl compounds.						
p-C_6H_4·OMe	155° *	$C_{14}H_{15}ON_3S$	61·3	5·5	61·5	5·4
p-C_6H_4·OEt	150 *	$C_{15}H_{17}ON_3S$	62·4	5·7	62·7	5·9
2 : 3-Xylyl	172 *	$C_{15}H_{17}N_3S$	66·3	6·3	66·4	6·2
p-$C_6H_4Bu^n$	134 *	$C_{17}H_{21}N_3S$	68·0	6·8	68·2	7·0
p-C_6H_4Cl	158 *	$C_{13}H_{12}N_3SCl$	55·9	4·1	56·2	4·3
p-C_6H_4Br	165 *	$C_{13}H_{12}N_3SBr$	48·1	3·9	48·4	3·7
α-$C_{10}H_7$	185 *	$C_{17}H_{15}N_3S$	69·8	5·2	69·6	5·1
1-Phenyl compounds.						
p-C_6H_4·OMe	169	$C_{14}H_{15}ON_3S$	61·2	5·2	61·5	5·4
p-C_6H_4·OEt	182	$C_{15}H_{17}ON_3S$	62·6	5·8	62·7	5·9
o-C_6H_4·OEt	185	$C_{15}H_{17}ON_3S$	62·4	5·9	62·7	5·9
p-C_6H_4·O·CH_2Bu^i	179	$C_{18}H_{23}ON_3S$	65·3	7·1	65·6	6·9
2 : 3-Xylyl	198	$C_{15}H_{17}N_3S$	66·1	6·1	66·4	6·2
2 : 4-Xylyl	173	$C_{15}H_{17}N_3S$	66·5	6·1	66·4	6·2
p-$C_6H_4Pr^n$	144	$C_{16}H_{19}N_3S$	67·5	6·8	67·3	6·6
p-$C_6H_4Bu^n$	152	$C_{17}H_{21}N_3S$	68·0	7·1	68·2	7·0
p-C_6H_4F	177	$C_{13}H_{12}N_3SF$	59·4	4·3	59·7	4·5
1-Phenyl compounds (contd.).						
p-C_6H_4Cl	176°	$C_{13}H_{12}N_3SCl$	55·9	4·5	56·2	4·3
p-C_6H_4Br	178	$C_{13}H_{12}N_3SBr$	48·1	3·8	48·4	3·7
α-$C_{10}H_7$ [a]	203	$C_{17}H_{15}N_3S$	—	—	—	—
p-Tolyl [b]	186	$C_{14}H_{15}N_3S$	—	—	—	—
1-Methyl-1-phenyl compounds.			N (%)		N (%)	
p-C_6H_4Cl	172	$C_{14}H_{14}N_3SCl$	14·3		14·4	
p-Tolyl	165	$C_{15}H_{17}N_3S$	15·1		15·4	
p-C_6H_4Et	162	$C_{16}H_{19}N_3S$	14·4		14·7	
2 : 4-Xylyl	172	$C_{16}H_{19}N_3S$	14·6		14·7	
p-C_6H_4·OEt	145	$C_{16}H_{19}ON_3S$	13·6		13·9	

* Sintering only, due to rapid rearrangement to the isomeric 1 : 4-derivative which occurs at the given temperature.

[a] Dixon (*J.*, 1892, 1020) gave m. p. 183°. [b] Von Walther and Stenz (*J. prakt. Chem.*, 1906, **74**, 229) gave m. p. 165°; Dixon [5] gave m. p. 173—174°; Marckwald [5] gave m. p. 176°.

Marckwald [5] and Dixon [5] both found that phenyl *iso*thiocyanate and phenylhydrazine gave 2 : 4-diphenylthiosemicarbazide in the cold, and the 1 : 4-isomer at high temperature, and Busch [6] showed this difference to arise from thermal rearrangement of the 2 : 4-compound. A number of aryl *iso*thiocyanates have now been found to react with phenylhydrazine according to the same pattern; in other cases, however, a 1 : 4-diarylthiosemicarbazide (IV) was obtained at both low and high temperature, the 2 : 4-isomer

$$\underset{\text{(III)}}{NH_2{\cdot}NPh{\cdot}CS{\cdot}NHAr} \longrightarrow \underset{\text{(IV)}}{NHPh{\cdot}NH{\cdot}CS{\cdot}NHAr}$$

(III) probably rearranging even in the cold. Table 3 records a number of 4-aryl-1-phenylthiosemicarbazides.

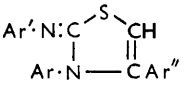
Aryl *iso*thiocyanates and thiosemicarbazide yielded 1-(arylaminothioformyl)thiosemicarbazides (V) (Table 4); 1-(arylaminothioformyl)semicarbazides (VI) were similarly

$$\underset{\text{(V)}}{Ar{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}NH{\cdot}CS{\cdot}NH_2} \qquad \underset{\text{(VI)}}{Ar{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}NH{\cdot}CO{\cdot}NH_2}$$

obtained with semicarbazide. The " symmetrical " formulæ (V) and (VI) are assumed because of the stability of those compounds to heat; the alternative unsymmetrical formulæ would correspond to compounds which would probably undergo thermal rearrangement.

Von Walther [7] found that ω-bromoacetophenone with thiocarbanilide gave 3 : 4-diphenyl-2-phenylimino-Δ^4-thiazoline, and this reaction has now been applied to some antiviral and tuberculostatic substituted thiocarbanilides. In every instance, only one of the two possible 3 : 4-diaryl-2-arylimino-Δ^4-thiazolines (VIII) was obtained; from the

$$\underset{\text{(VII)}}{Ar'{\cdot}N{:}C(SH){\cdot}NHAr}$$



(VIII)

results of von Walther's degradation of similar unsymmetrical compounds, it can be assumed that the arylimino-radical in the thiol form (VII) of unsymmetrical thiocarbanilides involves the more bulky aryl group.

Results of the antiviral tests with a number of compounds described herein have recently been reported elsewhere; [8] in tests for tuberculostatic properties *in vitro*, none of the compounds showed significant activity.

Experimental

M. p.s are the temperature of instantaneous fusion, determined on Maquenne and Kofler blocks.

Preparation of 4-Arylthiosemicarbazides.—To an ice-cooled solution of 95% hydrazine hydrate (2 mol.) in ethanol, the appropriate aryl *iso*thiocyanate (1 mol.) in ethanol was added in small portions with stirring; the condensation was generally strongly exothermic.[9] The solid precipitate of the 4-arylthiosemicarbazide formed in almost theoretical yield was washed with aqueous ethanol and recrystallised from ethanol. 4-p-*Fluorophenylthiosemicarbazide*, needles, m. p. 189° (Found : N, 22·5. $C_7H_8N_3SF$ requires N, 22·7%), gave 4-p-*fluorophenylthiosemicarbazones* from : *p*-chlorobenzaldehyde, needles, m. p. 205° (from ethanol–benzene) (Found : N, 13·6. $C_{14}H_{11}N_3SClF$ requires N, 13·6%); piperonaldehyde, prisms, m. p. 223° (from ethanol–benzene) (Found : N, 13·0. $C_{15}H_{12}O_2N_3SF$ requires N, 13·2%). Also prepared were : 4-p-*ethoxyphenyl-*, needles, m. p. 145° (Found : C, 50·9; H, 6·1. $C_9H_{13}ON_3S$ requires C, 51·1; H, 6·1%); 4-p-*ethylphenyl-*, needles, m. p. 131° (Found : N, 21·4. $C_9H_{13}N_3S$ requires

[5] Marckwald, *Ber.*, 1892, **25**, 3107; Dixon, *J.*, 1892, **61**, 1013.
[6] Busch, *Ber.*, 1909, **42**, 4599; Busch and Limpach, *Ber.*, 1911, **44**, 1579.
[7] Von Walther, *J. prakt. Chem.*, 1907, **75**, 188.
[8] Buu-Hoï, Gley, Bouffanais, Xuong, and Nam, *Experientia*, 1956, **12**, 73.
[9] Guha and Ray, *J. Amer. Chem. Soc.*, 1925, **47**, 387; Fromm, *Annalen*, 1926, **447**, 304.

N, 21·5%); 4-m-*chlorophenyl*-, leaflets, m. p. 115° (Found: N, 20·5. $C_7H_8N_3SCl$ requires N, 20·8%); 4-*p*-chlorophenyl-, m. p. 191° (Busch and Ulmer[10] gave m. p. 180°); 4-m-*tolyl*-, leaflets, m. p. 108° (Found: N, 23·0. $C_8H_{11}N_3S$ requires N, 23·2%), and 4-β-*naphthyl-thiosemicarbazide*, prisms, m. p. 178° (Found: N, 19·0. $C_{11}H_{11}N_3S$ requires N, 19·3%).

Preparation of 4-*Aryl*-1-(*arylaminothioformyl*)*thiosemicarbazides*.—A solution of the 4-arylthiosemicarbazide (1 mol.) in warm ethanol was treated with a solution of the appropriate aryl *iso*thiocyanate (1 mol.) in ethanol, and the product formed instantaneously was collected after

TABLE 4. 1-(*Arylaminothioformyl*)*thiosemicarbazides* (V).

Aryl	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
Ph [a]	218°	$C_8H_{10}N_4S_2$	—	—	—	—
p-Tolyl	222	$C_9H_{12}N_4S_2$	44·7	5·1	45·0	5·0
2 : 4-Xylyl	223	$C_{10}H_{14}N_4S_2$	46·8	5·4	47·2	5·5
2 : 3-Xylyl	198	$C_{10}H_{14}N_4S_2$	47·0	5·3	47·2	5·5
p-C_6H_4Et	218	$C_{10}H_{14}N_4S_2$	46·9	5·2	47·2	5·5
p-C_6H_4Pr^n	241	$C_{11}H_{16}N_4S_2$	49·0	6·0	49·2	5·9
p-C_6H_4Bu^n	223	$C_{12}H_{18}N_4S_2$	50·8	6·1	51·0	6·3
α-$C_{10}H_7$	229	$C_{12}H_{12}N_4S_2$	52·0	4·6	52·1	4·3
β-$C_{10}H_7$	218	$C_{12}H_{12}N_4S_2$	51·8	4·5	52·1	4·3
o-C_6H_4Ph	199	$C_{14}H_{14}N_4S_2$	55·3	4·5	55·6	4·6
p-C_6H_4·OMe	238	$C_9H_{12}ON_4S$	41·8	4·4	42·1	4·6
p-C_6H_4·OEt	241	$C_{10}H_{14}ON_4S_2$	44·3	4·9	44·4	5·1
p-C_6H_4·O·CH_2Bu^i	223	$C_{13}H_{20}ON_4S_2$	49·8	6·7	50·0	6·4
p-C_6H_4F	240	$C_8H_9N_2S_4F$	39·0	3·4	39·3	3·6
p-C_6H_4Cl	249	$C_8H_9N_2S_4Cl$	36·3	3·3	36·8	3·4
p-C_6H_4Br	241	$C_8H_9N_4S_2Br$	31·1	2·7	31·4	2·9

[a] Arndt, Milde, and Tschenscher (*Ber.*, 1922, **55**, 344) gave m. p. 180°; Mazurewitsch (*Bull. Soc. chim. France*, 1927, **41**, 647) gave m. p. 169—170° (decomp.).

TABLE 5. Δ^4-*Thiazolines* (VIII).

Ar	Ar′	Ar″	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
p-C_6H_4Cl	*p*-C_6H_4F	*p*-Tolyl [a]	157°	$C_{22}H_{16}N_2SClF$	66·8	4·0	66·9	4·0
2 : 5-$C_6H_3Cl_2$	,,	,,	122	$C_{22}H_{15}N_2SCl_2F$	61·2	3·3	61·5	3·4
p-C_6H_4·O·CH_2Bu^i	*p*-C_6H_4Et	,,	95	$C_{29}H_{32}ON_2S$	76·0	7·3	76·3	7·0
p-C_6H_4Cl	*p*-C_6H_4F	*p*-C_6H_4Cl [b]	195	$C_{21}H_{13}N_2SCl_2F$	60·6	3·2	60·7	3·1
2 : 5-$C_6H_3Cl_2$	,,	,,	130	$C_{21}H_{12}N_2SCl_3F$	55·7	2·8	56·0	2·6
p-C_6H_4·O·CH_2Bu^i	*p*-C_6H_4Et	,,	117	$C_{28}H_{29}ON_2SCl$	70·2	6·3	70·5	6·1
p-C_6H_4Cl	*p*-C_6H_4F	*p*-C_6H_4Br [c]	202	$C_{21}H_{13}N_2SBrClF$	54·6	2·6	54·8	2·8
2 : 5-$C_6H_3Cl_2$	,,	,,	163	$C_{21}H_{12}N_2SBrCl_2F$	50·2	2·3	51·0	2·4
p-C_6H_4·O·CH_2Bu^i	*p*-C_6H_4Et	,,	128	$C_{28}H_{29}ON_2SBr$	64·2	5·5	64·5	5·6

Triads prepared from (*a*) ω-bromo-4-methylacetophenone, (*b*) ω-bromo-4-chloroacetophenone, and (*c*) 4 : ω-dibromoacetophenone.

cooling, washed with ethanol, and recrystallised from ethanol or ethanol–benzene. The substances obtained formed needles or leaflets, which decomposed when heated gradually, so that the m. p.s varied widely according to the speed of heating.

Preparation of 4-*Aryl*-1-(*arylaminoformyl*)*thiosemicarbazides*.[11]—A cooled solution of the 4-arylthiosemicarbazide (1 mol.) in ethanol was treated with a benzene solution of the appropriate *iso*cyanate (1 mol.) with stirring; the precipitate formed in almost theoretical yield was washed with ethanol and recrystallised from ethanol (in which it was only sparingly soluble) or ethanol–benzene. Remarks as above apply to the m. p.s of these compounds.

1-(p-*Ethoxyphenylaminoformyl*)*semicarbazide*.—*p*-Ethoxyphenyl *iso*thiocyanate (3 g.) in ethanol was added to a cold ethanol solution of semicarbazide (prepared from 2·5 g. of the hydrochloride and sodium acetate); the precipitated *product* formed leaflets, m. p. 243°, from ethanol (Found: N, 21·7. $C_{10}H_{14}O_2N_4S$ requires N, 22·0%). 1-(p-*Fluoroanilinothioformyl*)-*semicarbazide*, similarly prepared from *p*-fluorophenyl *iso*thiocyanate, formed needles, m. p. 246—247°, from ethanol–benzene (Found: N, 24·8. $C_8H_9ON_4SF$ requires N, 24·6%).

Condensation of Aryl iso*Thiocyanates with Phenylhydrazine*.—This was effected in cooled ethanol for 4-aryl-2-phenylthiosemicarbazides, and in hot ethanol for the 4-aryl-1-phenylthiosemicarbazides; the former compounds were recrystallised in cold, and the latter in boiling,

[10] Busch and Ulmer, *Ber.*, 1902, **35**, 1715.
[11] Cf. Bülow and Sautermeister, *Ber.*, 1906, **39**, 651.

ethanol. In all the cases where the 2 : 4-derivative could be prepared, it was found to undergo rearrangement on recrystallisation from boiling ethanol or benzene.

Condensation of ω-Bromo-ketones with NN'*-Diarylthioureas.*—Equimolar amounts of the reagents were heated in boiling ethanol for a few hours, the precipitate which formed on cooling was basified with aqueous sodium hydroxide, and the 3 : 4-diaryl-2-arylimino-Δ^4-thiazoline obtained was recrystallised from ethanol.

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