

Organic Pesticides. Part X. Preparation of Some 2-Amino-4-aryl-5-alkylthiazoles and Related Compounds, *N*-Substituted Aminothiazoles and their Mercurials, and 2-*p*-Fluorophenylimino-4-thiazolidone and its Condensation Products

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A number of substituted 2-aminothiazoles and their condensation products with *p*-fluorobenzenesulphonyl chloride and 2-methyl-5-fluorobenzenesulphonyl chloride, *N*-substituted aminothiazoles and their mercury derivatives, 2-acetamino-4-aryl-5-thiazole sulphonamides, and 2-*p*-fluorophenylimino-4-thiazolidone and its condensation products with different aldehydes have been synthesised with a view to studying their pesticidal properties.

The fungicidal activity of well-known organic sulphur fungicides like tetramethylthiuram disulphide, substituted thiourcas, and thiosemicarbazides is attributed to the presence of the N-C-S group¹. This group is also present in thiazoles and thiazolidones and several substituted compounds of this type have pronounced fungicidal toxicity. In continuation of the work on fluoro-substituted thiazoles, carried out in our laboratories,² we have extended the work to synthesise a number of substituted thiazoles and thiazolidones as potential pest-control chemicals.

2-Amino-4-aryl-5-alkylthiazoles have been prepared by condensing the appropriate fluorinated ketones with thiourea in presence of iodine by the method of King and Hlavacek³. These have been heated with acetic anhydride to give the corresponding acetyl derivatives⁴ and condensed with *p*-fluorobenzenesulphonyl chloride and 2-methyl-5-fluorobenzenesulphonyl chloride⁴ to furnish the corresponding arylsulphonamidothiazoles. One typical case has been illustrated in the Experimental.

N-Substituted aminothiazoles have been similarly prepared by the condensation of fluorinated ketones in presence of iodine with α -*p*-fluorophenylthiourea and the products have been mercurated by the method of Pujari and Rout⁵ with a view to enhancing their toxicity as similar mercurated compounds are known to be effective fungicides. In view of some of the earlier observations on the mercuration of aromatic amines and phenols⁶, it has been presumed that the acetoxymercuri group enters the *ortho* position (with respect

1. Goldsworth, *Phytopath.*, 1942, **32**, 497.

2. Joshi and Giri, *this Journal*, 1961, **38**, 117; 1962, **39**, 17.

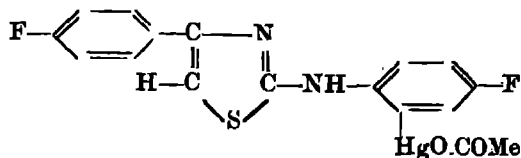
3. *J. Amer. Chem. Soc.*, 1950, **72**, 3722.

4. Das and Rout, *this Journal*, 1955, **32**, 063.

5. *Ibid.*, 1954, **31**, 257.

6. Newton Friend, "Text Book of Inorganic Chemistry, Part I"; Guha Sircar *et al.*, *this Journal*, 1952, **29**, 768, 770; 1950, **27**, 535 *et seq.*

to -NH group) of the aryl nucleus in the thiazole base since the *para* position is blocked by a fluorine atom. Thus the mercurated thiazole bases are considered to possess the structure :



Further, 2-acetamino-4-*p*-fluorophenylthiazole and 2-acetamino-4-(2'-fluoro-5'-*π*-ethyl)-phenylthiazole have been chlorosulphonated by the method of Das and Rout⁷ to give the corresponding sulphonyl chlorides which have subsequently been condensed with concentrated NH_4OH , aniline, and *p*-fluoroaniline. One synthesis has been illustrated in the Experimental as an example.

Lastly, 2-*p*-fluorophenylimino-4-thiazolidone has been prepared by the condensation of α -*p*-fluorophenylthiourea with monochloroacetic acid in absolute ethanol in presence of anhydrous sodium acetate⁷. It has been then mercurated and also condensed with eight different aldehydes in glacial acetic acid medium in presence of fused sodium acetate. A typical example has been described in the Experimental.

EXPERIMENTAL

The seven aromatic fluorinated ketones used were prepared by the method of Bui-Hoi and Xuong⁸.

2-Amino-4-*p*-fluorophenylthiazole (I).—A mixture of *p*-fluoroacetophenone (5 g.), thiourea (5.5 g.), and iodine (9 g.) was heated on a water bath for 60 hours. It was kept in contact with ether for 24 hours; the ether was then decanted and the residue washed with a solution of sodium thiosulphate followed by water. The residue was then boiled with water, ammonia (conc.) added to it, and the mixture cooled. The solid separating was filtered, washed, and recrystallised from aqueous ethanol, m.p. 120°, yield 6 g. (85.7% of theory).

2-Acetamino-4-*p*-fluorophenylthiazole (II).—Compound (I, 2 g.) was refluxed with acetic anhydride (20 ml) for 2 hours; the mixture was cooled and poured into ice-water. The solid separating was filtered, washed, and recrystallised from ethanol, m.p. 212°, yield 2.25 g. (90.1% of theory). The compounds thus prepared are listed in Table I.

p-Fluorobenzenesulphonyl chloride and 2-methyl-5-fluorobenzenesulphonyl chloride were prepared by following the method of Huntress and Carten⁹.

4-(*p*-Fluorophenyl)-2-*p*-fluorophenylsulphonamidothiazole.—Compound (I, 2 g.) and *p*-fluorobenzenesulphonyl chloride (2 g.) were heated under reflux with dry pyridine (20 ml) at 65–70° for 3 hours. After cooling, the mixture was diluted with water when a gummy

7. Rout and Mahapatra, *J. Amer. Chem. Soc.*, 1955, **77**, 2426.

8. *J. Chem. Soc.*, 1953, 386.

9. *J. Amer. Chem. Soc.*, 1940, **62**, 611.

product appeared. It was dissolved in ammonia (conc.) and reprecipitated by adding HCl(dil.) when a solid separated. It was filtered, washed with water, and recrystallised from ethanol, m. p. 155° (decomp.), yield 2 g. (55.6% of theory).

In some cases, the gummy product could not be induced to solidify. The compounds prepared have been recorded in Table II.

α -*p*-Fluorophenylthiourea was prepared by the method of Blatt¹⁰. It was condensed with different ketones by the usual method to yield *N*-substituted aminothiazoles and the latter were mercurated (*vide infra*).

4-*p*-Fluorophenyl-2-(4'-fluoro-2'-acetoxymercuri)-phenylaminothiazole.—To 4-*p*-fluorophenyl-2-*p*-fluorophenylaminothiazole (1.5 g.), dissolved in ethanol-acetic acid medium, a solution of mercuric acetate (2 g.) in water-acetic acid medium was added; the mixture was shaken well, kept overnight, filtered, and washed with hot water, dilute acetic acid, and ethanol; m.p. 237°, yield 2 g. (70% of theory). The compounds obtained are listed in Table III.

2-Acetamino-4-*p*-fluorophenyl-5-thiazole Sulphonyl Chloride (III).—Chlorosulphonic acid (70 g.) was taken in a flask, kept immersed in an ice-bath. To this compound (II) (17 g.) was added at intervals. It was shaken after every addition. The mixture was heated on a water bath for 3 hours, cooled, and poured on broken ice. It was stirred and the solid separating was collected, washed, and dried in *vacuo*, m.p. 155° (decomp.), yield 13g. (59.2% of theory).

2-Acetamino-4-*p*-fluorophenyl-5-thiazole Sulphonamide.—A mixture of the compound (III) (3 g.) and ammonia (conc., 9ml) was heated on a water bath for 2 hours, cooled, and acidified with H₂SO₄ (dil.). The solid separating was filtered, washed, and dried in *vacuo*; m.p. 230° (decomp.), yield 2 g. (70.8% of theory).

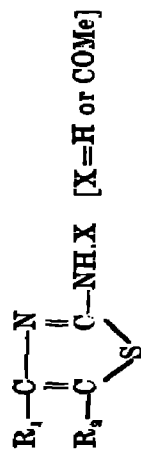
4-*p*-Fluorophenyl-2-acetamino-5-phenylsulphonamidothiazole.—A mixture of compound (III) (3 g.), aniline (1 g.), and dry pyridine (30 ml) was heated on a water bath for 3 hours, cooled, and diluted with water. The supernatant liquid was decanted and the sticky residue left was kept for 24 hours in contact with a large excess of ether. After decanting the ether, the compound was dried in *vacuo*, m.p. 240°, yield 0.5 g. (13% of theory). The compounds prepared have been listed in Table IV.

2-*p*-Fluorophenylimino-4-thiazolidone (IV).—A mixture of α -*p*-fluorophenylthiourea (5.1g.), monochloroacetic acid (3 g.), anhydrous sodium acetate (3 g.), and absolute ethanol (25ml) was refluxed for 4 hours, cooled, and poured on water. It was filtered, washed several times with hot water, and recrystallised from ethanol, m.p. 185°, yield 3g. (48.6% of theory). (Found: S, 15.03. C₉H₇O₂N₂FS requires S, 15.23%).

2-(4'-Fluoro-2'-acetoxymercuri)-phenylimino-4-thiazolidone.—To compound (IV) (1g.), dissolved in EtOH-AcOH medium, an aqueous solution of mercuric acetate (2 g.) in water (30ml) was added; the mixture was shaken well and kept overnight. It was filtered and washed well with hot water, dilute acetic acid, and ethanol, m.p. 280°, yield 2g. (89.7%). (Found: S, 6.65; Hg, 42.58. C₁₁H₉O₄N₂FSHg requires S, 6.83; Hg, 42.73%).

10. "Organic Syntheses, Part III", p. 735.

TABLE I



2-Amino-4-aryl-5-alkylthiazoles.

Compd. No.	R ₁ .	R ₂ .	Yield.	M.P.	Formula.	% Sulphur.		Acetyl derivatives.			
						Found	Reqd.	Yield.	M.P.	% Sulphur.	Found.
1	<i>p</i> -Fluorophenyl	H	85.7%	120°	C ₉ H ₇ N ₂ FS	16.32	16.49	90.1%	212°(d)	13.29	13.55
2	Do	Me	96.1	127°	C ₁₀ H ₉ N ₂ FS	15.59	15.38	91.7	215°	12.62	12.80
3	3'-Methyl-4'-fluorophenyl	H	83.3	87°	C ₁₀ H ₉ N ₂ FS	15.16	15.38	83.3	190°(d)	13.08	12.80
4	2'-Fluoro-5'-methyl-phenyl	H	60.0	110°	C ₁₀ H ₉ N ₂ FS	15.63	15.38	96.0	230°(d)	13.03	12.80
5	<i>p</i> -Fluorophenyl	Et	48.0	90°	C ₁₁ H ₁₁ N ₂ FS	14.25	14.41	84.0	188°(d)	12.34	12.11
6	2'-Fluoro-5'-methylphenyl	Me	69.4	100°	C ₁₁ H ₁₁ N ₂ FS	14.30	14.41	91.6	164°	11.88	12.11
7	Do	Et	59.3	119°	C ₁₂ H ₁₃ N ₂ FS	13.78	13.55

(d) denotes decomposition.

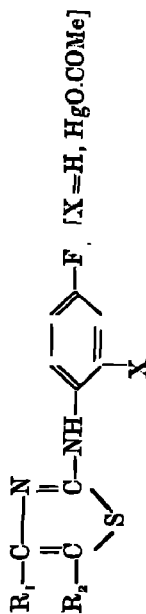
TABLE II

Condensation with *p*-fluorobenzeneisulphonyl chloride and 2-methyl-5-fluorobenzeneisulphonyl chloride.

*Compd. No.	X = C ₆ H ₄ F.			X = C ₆ H ₃ { F(1) / Me(4) }		
	Yield.	M.P.	% Sulphur.	Yield.	M.P.	% Sulphur.
			Found.			Found.
1	55.6%	155° (d)	18.02	25.0%	67°	17.05
2	90°	..
3	66.0	122°	17.24	83.3	134°	16.24
4	45.4	216°	17.20	..	206° (d)	..
5	Gum	..
6	35.1	165° (d)	17.16	..	Do	..
7	Do	..

*The natures of R₁ and R₂ are same as in Table I. (d) denotes decom position.

TABLE III



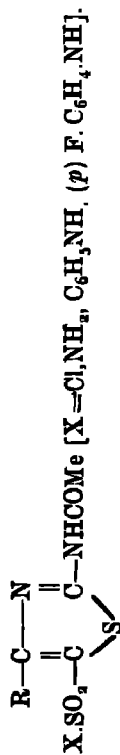
Compd. No.	R ₁	R ₂	Yield.	M.P.	Formula.	%Sulphur.		Yield.	M.P.	Formula.	% Sulphur.	
						Found.	Reqd.				Found.	Reqd.
1	<i>p</i> -Fluorophenyl	H	48.0%	110°	C ₁₅ H ₁₀ N ₂ F ₂ S	11.36	11.11	70 %	237°	C ₁₇ H ₁₂ O ₂ N ₂ F ₂ SHg	36.28	36.63
2	<i>p</i> -Fluorophenyl	Me	42.5	77°	C ₁₆ H ₁₂ N ₂ F ₂ S	10.29	10.59	27	•	C ₁₈ H ₁₄ O ₂ N ₂ F ₂ SHg	35.28	35.71
3	3'-Methyl-4'-fluorophenyl	H	57.0	80°	C ₁₆ H ₁₂ N ₂ F ₂ S	10.72	10.59	35.7	300°	C ₁₈ H ₁₄ O ₂ N ₂ F ₂ SHg	35.23	35.71
4	2'-Fluoro-5'-methylphenyl	H	42.0	48°	C ₁₆ H ₁₂ N ₂ F ₂ S	10.76	10.59	27	120°	C ₁₈ H ₁₄ O ₂ N ₂ F ₂ SHg	35.19	35.71
5	<i>p</i> -Fluorophenyl	Et	35.0	40°	C ₁₇ H ₁₄ N ₂ F ₂ S	9.93	10.12	27	•	C ₁₉ H ₁₆ O ₂ N ₂ F ₂ SHg	34.46	34.84

4-Aryl-5-alkyl-2-*p*-fluorophenylaminothiazole.

4-Aryl-5-alkyl-2-(4'-fluoro-2'-acetoxymercuri)-phenylaminothiazole.

*Decomposes but does not melt.

TABLE IV



Compd. No.	R.	Yield.	M.P.	%Sulphur.	Found.	Reqd.	X=NH ₂ .		X=C ₆ H ₅ NH ₂ .		X=(<i>p</i>)F.C ₆ H ₄ NH ₂ .				
							Corr. sulphona amide.	M.P.	Yield.	%Sulphur.	Corr. phenylsulphonamide.	Yield.	%Sulphur.	Corr. <i>p</i> -fluorophenylsulphonamide.	Yield.
1	<i>p</i> -Fluorophenyl	59.2%	155°(d)	18.96	19.13	20.63	20.31	13.0%	240°	16.63	16.36	25.0%	217°	15.32	15.64
2	2'-Fluoro-5'-methyl	84.3	125°(d)	18.06	18.36	72.4	180°(d)	40.0	90°	15.46	15.80	43.6	260°	15.50	15.13

X=Cl.

2-Acetamino-4-aryl-5-thiazole sulphonyl chloride.

TABLE V

Condensation products of different aldehydes with 2-p-fluorophenylimino-4-thiazolidone.

Compd. No.	Aldehyde.	Colour.	Yield.	M.P.	Formula.	% Sulphur. Found.	% Sulphur. Reqd.
1	<i>p</i> -Nitrobenzaldehyde	Brick-red	91.3%	> 285°	C ₁₆ H ₁₀ O ₃ N ₃ FS	9.56	9.27
2	Benzaldehyde	Pale yellow	52.8	277°	C ₁₆ H ₁₁ O ₂ N ₂ FS	10.32	10.73
3	Salicylaldehyde	Distinct yellow	68.8	218°	C ₁₆ H ₁₁ O ₂ N ₂ FS	10.58	10.19
4	<i>p</i> -Hydroxybenzaldehyde	Pale yellow	66.8	228°	C ₁₆ H ₁₁ O ₂ N ₂ FS	9.86	10.19
5	Anisaldehyde	Do	64.0	255°	C ₁₇ H ₁₃ O ₂ N ₂ FS	10.16	9.75
6	Vanillin	Do	61.0	205°	C ₁₇ H ₁₃ O ₃ N ₂ FS	8.88	9.30
7	Cinnamaldehyde	Distinct yellow	64.6	230° (d)	C ₁₈ H ₁₄ O ₂ N ₂ FS	9.63	9.84
8	<i>p</i> -Dimethylamino-benzaldehyde	Light brown	61.2	260°	C ₁₈ H ₁₆ ON ₂ FS	9.16	9.38

d = decomposes.

(5-Benzylidene-2-p-fluorophenylimino-4-thiazolidone.—A mixture of the compound (IV) (2g.), benzaldehyde (1.2g.), fused sodium acetate (3 g.), and glacial acetic acid (50 ml) was refluxed directly on a wire-gauge. The solution soon became clear and again turned turbid after refluxing for 2½ hours when a solid separated. The mixture was cooled, poured on water, and left overnight. It was filtered, washed, and recrystallised from ethanol as a pale yellow solid, m.p. 277°, yield 1.5 g. (52.8% of theory). The compounds prepared thus have been recorded in Table V.

The pesticidal activity of these compounds is under investigation and will be communicated in due course.

Thanks of the authors are due to the Council of Scientific and Industrial Research, New Delhi, for the award of a junior research fellowship to one of them (S.C.B.) and to Dr. R.C. Mehrotra, Professor and Head of the Department of Chemistry, University of Gorakhpur, for providing all departmental facilities.

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Errata

In Part IX of this series, published in the January issue, 1962, in column I of Table II, p. 19, compounds 4 to 8 should be read as 5 to 9 as compound 4 in Table I was not mercurated.