803. *The Preparation of Some Aryl Pyrazolyl Sulphides.*

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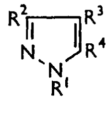
Hydrazines have been condensed with thio-β-diketones to form the pyrazolyl sulphides (I—III) and (VIII—X). These sulphides were also prepared by the action of *o*-nitrobenzenesulphenyl chloride on the corresponding pyrazoles in solvents, and by a novel technique of melting together the two reactants. Hydrolysis of the 1-pyrazolyl sulphides (XI—XVI) has been investigated.

3-*o*-NITROPHENYLTHIOPENTANE-2,4-DIONE,[1] 2-*o*-nitrophenylthio-1-phenylbutane-1,3-dione,[1] and 2-*o*-nitrophenylthio-1,3-diphenylpropane-1,3-dione [1] react with phenylhydrazine to form, respectively, the phenylpyrazolyl sulphides (I—III), and with hydrazine to form, respectively, the pyrazolyl sulphides (VIII—X). The sulphides (I—III) were also prepared by reaction between *o*-nitrobenzenesulphenyl chloride [2] and the corresponding pyrazole in ethylene dichloride without the use of a catalyst. This direct attack of the sulphur reagent is interesting since it is a second example, the previous case being formation of a sulphoxide by thionyl chloride.[3] The sulphides (V—VII) were prepared in a similar manner, but sulphide (IV) could not be obtained from 1-phenylpyrazole.[4] The sulphides (I—VII) were also prepared by the novel technique of melting together *o*-nitrobenzenesulphenyl chloride with the corresponding pyrazole, leading to higher yields and also successful reaction with 1-phenylpyrazole.



	R^1	R^2	R^3	R^4
(I)	Ph	Me	SAr	Me
(II)	Ph	Me	SAr	Ph
(III)	Ph	Ph	SAr	Ph
(IV)	Ph	H	SAr	H
(V)	Ph	H	SAr	Me
(VI)	Ph	Me	SAr	H
(VII)	Ph	Ph	SAr	Me
(VIII)	H	Me	SAr	Me
(IX)	H	Me	SAr	Ph
(X)	H	Ph	SAr	Ph
(XI)	SAr	Me	SAr	Me
(XII)	SAr	Me	SAr	Ph
(XIII)	SAr	Ph	SAr	Ph
(XIV)	SAr	Me	H	Me
(XV)	SAr	Me	H	Ph
(XVI)	SAr	Ph	H	Ph

Ar = o-$NO_2 \cdot C_6H_4$.

Reaction of *o*-nitrobenzenesulphenyl chloride with *N*-unsubstituted pyrazoles was more complicated. *o*-Nitrobenzenesulphenyl chloride and 3,5-dimethylpyrazole [5] in ethylene dichloride formed the sulphide (XI), but attempts to prepare sulphides (VIII—X), (XII), (XIII) in a similar manner failed. However, melting *o*-nitrobenzenesulphenyl chloride with the corresponding pyrazole gave the sulphides (VIII—X). The sulphides (XI—XIII) were obtained by the action of *o*-nitrobenzenesulphenyl chloride on the sulphides (VIII—X) in ether containing pyridine; and the sulphides (XIV—XVI) were obtained similarly. In these cases (XI—XVI) the pyrazoles behave similarly to secondary amines.[6]

The N–S bond in the sulphides (XI—XVI) was readily hydrolysed by 90% aqueous acetic acid (cf. secondary amines [6]). Hydrolysis of sulphides (XIV—XVI) gave the corresponding pyrazole and di-*o*-nitrophenyl disulphide,[7] whereas that of the sulphides (XI—XIII) gave the corresponding sulphides (VIII—X) but no disulphides. Further, it is interesting that in no case was *o*-nitrophenyl *o*-nitrobenzenethiolsulphonate [8] isolated.

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[1] Finar and Montgomery, *J.*, 1961, 367.
[2] Hubacher, *Org. Synth.*, Coll. Vol. II, 1943, p. 455.
[3] Finar and Lord, *J.*, 1959, 1819.
[4] Finar and Hurlock, *J.*, 1957, 3024.
[5] Rothenburg, *Ber.*, 1894, **27**, 1097.
[6] Billman and Mahoney, *J. Amer. Chem. Soc.*, 1939, **61**, 2340.
[7] Mohlau, Beyschlag, and Kohser, *Ber.*, 1912, **45**, 131.
[8] Zincke and Farr, *Annalen*, 1912, **391**, 57.

Addition of *o*-nitrobenzenesulphenyl chloride to acetanilide in acetic acid gives *o*-nitrophenyl *o*-nitrobenzenethiolsulphonate. In a previous paper,[9] it was reported that the compound was di-*o*-nitrophenyl disulphone, since the analysis apparently corresponded to this structure. Repetition has shown, however, that the compound is actually *o*-nitrophenyl *o*-nitrobenzenethiolsulphonate. The melting point corresponded to that given previously,[9] but a new analysis corresponded to the thiolsulphonate. (Beilstein's " Handbuch " gives m. p. 142—143°; Kurzer and Tertiuk [10] give m. p. 139—141°; we found m. p. 147—148°.) Di-*o*-nitrophenyl disulphone has been prepared by the oxidation of *o*-nitrobenzenesulphinic acid [11] in acetic acid with potassium permanganate.[12] Addition of *o*-nitrobenzenesulphenyl chloride to acetanilide, in ether, in the presence of pyridine, gives *N*-(*o*-nitrophenylthio)acetanilide. This, on hydrolysis with aqueous acetic acid, regenerates acetanilide; 2,2'-dinitrodiphenyl disulphide is also formed, but no *o*-nitrophenyl *o*-nitrobenzenethiolsulphonate.

EXPERIMENTAL

Reaction of Arylthio-diketones with Phenylhydrazine.—A solution of 3-*o*-nitrophenylthiopentane-2,4-dione [1] (12·65 g., 0·05 mole) and phenylhydrazine (5·4 g., 0·05 mole) in ethanol (70 c.c.) and glacial acetic acid (35 c.c.) was heated on a steam-bath for 1·5 hr. Water was added to the hot solution and, after storage, the yellow precipitate was collected, washed with water, and recrystallised from aqueous acetic acid, giving pale yellow needles of 3,5-*dimethyl-*4-o-*nitrophenylthio-*1-*phenylpyrazole* (I), m. p. 149—150°. *Sulphides* (II) and (III) were prepared similarly (see Table 1).

Reactions of Arylthio-diketones with Hydrazine.—A solution of 2-*o*-nitrophenylthio-1,3-diphenylpropane-1,3 dione [1] (3·8 g., 0·01 mole) and hydrazine hydrate (0·5 g., 0·01 mole) in acetic acid (15 c.c.) was heated on a steam-bath for 2·5 hr. After storage, the yellow precipitate was collected and recrystallised from aqueous acetic acid, giving yellow cubes of 4-o-*nitrophenylthio-*3,5-*diphenylpyrazole* (X), m. p. 234·5—236°. *Sulphides* (VIII) and (IX) were prepared similarly (see Table 1).

TABLE 1.

Arylthiopyrazoles.

		Yield	Found (%)					Required (%)			
Compound	M. p.	(%)	C	H	N	S	Formula	C	H	N	S
(I)	149—150°	94	62·2	4·4	12·8	9·4	$C_{17}H_{15}N_3O_2S$	62·7	4·65	12·9	9·85
(II)	181—182	96	68·4	4·4	10·7	8·4	$C_{22}H_{17}N_3O_2S$	68·2	4·4	10·85	8·3
(III)	172—173	80	71·8	4·2	9·0	6·7	$C_{27}H_{19}N_3O_2S$	72·1	4·3	9·4	7·1
(VIII)	170—171	78	52·6	4·3	16·4	12·4	$C_{11}H_{11}N_3O_2S$	53·0	4·45	16·9	12·9
(IX)	150—151	82	61·75	4·3	13·1	10·0	$C_{16}H_3N_3O_2S$	61·7	4·2	13·5	10·3
(X)	234·5—236	91	67·6	4·0	11·5	9·0	$C_{21}H_{15}N_3O_2S$	67·5	4·05	11·3	8·6

Reaction of o-*Nitrobenzenesulphenyl Chloride with* 1-*Phenylpyrazoles.*—(i) *o*-Nitrobenzenesulphenyl chloride [2] (1·9 g., 0·01 mole) and 3,5-dimethyl-1-phenylpyrazole [13] (1·7 g., 0·01 mole) in ethylene dichloride (10 c.c.) were refluxed until hydrogen chloride ceased to be evolved (8 hr.). The solvent was distilled off and the solid recrystallised from aqueous acetic acid, giving the sulphide (I). *Sulphides* (II), (III), and (V—VII) were prepared similarly (see Table 2).

(ii) A mixture of *o*-nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) and 3,5-dimethyl-1-phenylpyrazole (1·7 g., 0·01 mole) was heated on a hot-plate at 120—130° until hydrogen chloride ceased to be evolved and the melt solidified (4 hr.). The solid recrystallised from aqueous acetic acid, giving the sulphide (I). Sulphides (II—VII) were prepared similarly (see Table 2).

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[9] Finar and Montgomery, *J.*, 1960, 483.

[10] Beilstein's " Handbuch der organischen Chemie," Hauptwerk, Vol. VI, p. 157; Kurzer and Tertiuk, *J.*, 1958, 1571.

[11] Claasz, *Annalen*, 1911, **380**, 314.

[12] Hilditch, *J.*, 1908, **93**, 1526.

[13] Knorr, *Ber.*, 1887, **20**, 1103.

TABLE 2.

Further arylthiopyrazoles.

Compound	Method	M. p.	Yield (%)	Found (%) C	Found (%) H	Found (%) N	Found (%) S	Formula	Required (%) C	Required (%) H	Required (%) N	Required (%) S
(I)	i	149—150°	72									
	ii		77									
(II)	i	181—182	75									
	ii		78									
(III)	i	172—173	61									
	ii		67									
(IV)	i	119—120	—	60·2	3·3	13·8	10·4	$C_{15}H_{11}N_3O_2S$	60·6	3·7	14·15	10·8
	ii		66									
(V)	i	99—100	76	61·5	3·9	13·6	10·6	$C_{16}H_{13}N_3O_2S$	61·7	4·2	13·5	10·3
	ii		77									
(VI)	i	105—106	71	61·4	4·0	13·4	10·4	$C_{16}H_{13}N_3O_2S$	61·7	4·2	13·5	10·3
	ii		74									
(VII)	i	187—188	76	68·0	4·1	10·4	8·0	$C_{22}H_{17}N_3O_2S$	68·2	4·4	10·85	8·3
	ii		84									

Reaction of o-*Nitrobenzenesulphenyl Chloride with* N-*Unsubstituted Pyrazoles.*—(*a*) A solution of *o*-nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) and 3,5-dimethylpyrazole[5] (1·0 g., 0·01 mole) in ethylene dichloride (10 c.c.) was refluxed until evolution of hydrogen chloride ceased (8 hr.). The solvent was distilled off and the solid recrystallised from chloroform–light petroleum, giving pale yellow cubes of 3,5-dimethyl-1,4-di-*o*-nitrophenylthiopyrazole (XI), m. p. 234—235°. Under similar conditions 3-methyl-5-phenylpyrazole[14] was precipitated as its hydrochloride and 3,5-diphenylpyrazole[15] was insoluble.

(*b*) When a mixture of *o*-nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) and 3,5-dimethylpyrazole (1·0 g., 0·01 mole) was heated on a hot-plate at 120—130° for 10 min., the melt solidified. The solid was recrystallised from chloroform–light petroleum, to give the sulphide (VIII). Sulphides (IX) and (X) were prepared similarly (see Table 3).

(*c*) *o*-Nitrobenzenesulphenyl chloride (3·8 g., 0·02 mole) and 3,5-dimethylpyrazole (1·0 g., 0·01 mole) in ethylene dichloride (10 c.c.) were refluxed on a steam-bath until evolution of hydrogen chloride ceased (8 hr.). The solid was collected and recrystallised from chloroform–light petroleum, giving the sulphide (XI). 3-Methyl-5-phenylpyrazole and 3,5-diphenylpyrazole behaved as before [see paragraph (*a*)].

(*d*) *o*-Nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) in ether (20 c.c.) was added to 3,5-dimethylpyrazole (1·0 g., 0·01 mole) in ether (20 c.c.) and pyridine (2 c.c.). The precipitate was collected and washed with ether (2 × 10 c.c.) and the combined filtrates were evaporated to half-volume. The solid was recrystallised from ether, to give yellow needles of 3,5-*dimethyl*-1-o-*nitrophenylthiopyrazole* (XIV), m. p. 112—113°. *Sulphides* (XV) and (XVI) were prepared similarly (see Table 3).

(*e*) A solution of the pyrazolyl sulphide (VIII) (2·5 g., 0·01 mole) and *o*-nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) in ethylene dichloride (10 c.c.) was heated on a steam-bath (2 hr.), and the solid collected and recrystallised from chloroform–light petroleum, giving the sulphide (XI). Under similar conditions sulphides (IX) and (X) were precipitated as their hydrochlorides (see Table 3).

(*f*) *o*-Nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) in ether (20 c.c.) was added to the pyrazolyl sulphide (IX) (3·1 g., 0·01 mole) in ether (30 c.c.) and pyridine (2 c.c.). The yellow precipitate was collected, washed with water, dried, and recrystallised from chloroform–light petroleum, giving yellow cubes of 3-*methyl*-1,4-*di*-o-*nitrophenylthio*-5-*phenylpyrazole* (XII), m. p. 203—204°. The sulphides (XI) and (XIII) were prepared similarly (see Table 3).

Hydrolysis of Pyrazolyl Sulphides (XI—XIII).—The sulphide (XIII) (1 g.) was refluxed in acetic acid (50 c.c.) and water (5 c.c.) for 10 min. Water was added to the hot solution, to give yellow plates of sulphide (X). Sulphides (XI) and (XII) behaved in a similar manner (see Table 4).

Hydrolysis of Pyrazolyl Sulphides (XIV—XVI).—The sulphide (XV) (3·1 g., 0·01 mole) was heated in acetic acid (50 c.c.) and water (10 c.c.) on the steam-bath for 1 hr. Water was added

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[14] Sjollema, *Annalen*, 1894, **279**, 248.

[15] Moureu and Brachin, *Compt. rend.*, 1903, **136**, 1264.

to the hot solution to give yellow needles of di-*o*-nitrodiphenyl disulphide,[7] m. p. 195—197°. The filtrate was extracted with chloroform (2 × 25 c.c.), the chloroform extract was evaporated to dryness and taken up in methanol, and a saturated solution of picric acid in ethanol added, giving a yellow precipitate of 3-methyl-5-phenylpyrazole picrate, m. p. 159°. Sulphides (XIV) and (XVI) behaved in a similar manner (see Table 4).

Reaction between o-*Nitrobenzenesulphenyl Chloride and Acetanilide.*—To a solution of *o*-nitrobenzenesulphenyl chloride (5·7 g., 0·03 mole) and acetanilide (4·1 g., 0·03 mole) in ether (200 c.c.) was added pyridine (2·3 g., 0·03 mole), and the whole was refluxed for 1·5 hr. On storage a precipitate was formed, which was discarded; the filtrate was evaporated to dryness, and the residue was washed with boiling ethanol, insoluble material being discarded. On cooling, the ethanolic solution yielded yellow crystals of N-(o-*nitrophenylthio*)*acetanilide*, m. p. 118—119° (35%) (Found: C, 58·5; H, 4·5; N, 9·5; S, 10·7. $C_{14}H_{12}N_2O_3S$ requires C, 58·3; H, 4·2; N, 9·7; S, 11·1%).

Hydrolysis of N-o-*Nitrophenylthioacetanilide.*—*N*-*o*-Nitrophenylthioacetanilide (1 g.) was refluxed in acetic acid (20 c.c.) and water (2 c.c.) for 1·5 hr. On cooling, the yellow crystals of di-*o*-nitrodiphenyl disulphide which separated were collected and dried (m. p. 194—196°; 0·3 g.). Evaporation of the filtrate left a brown solid which on recrystallisation from boiling water (charcoal) gave acetanilide, m. p. 112—113° (0·35 g.).

TABLE 3.

Further arylthiopyrazoles.

Starting pyrazole *	Method	Product	Yield (%)	M. p.
3,5-Me_2	*a*	XI	88	234—235°
,,	*b*	VIII	81	170—171
,,	*c*	XI	89	234—235
,,	*d*	XIV	83	112—113
3,5-Me_2-4-Ar	*e*	XI	89	234—235
,,	*f*	XI	89	234—235
3-Me-5-Ph	*a*	—		
,,	*b*	IX	68	150—151
,,	*c*	—		
,,	*d*	XV	68	124—126
3-Me-5-Ph-4-Ar	*e*	—		
,,	*f*	XII	96	203—204
3,5-Ph_2	*a*	—		
,,	*b*	X	44	234·5—236
,,	*c*	—		
,,	*d*	XVI	79	154—160
3,5-Ph_2-4-Ar	*e*	—		
,,	*f*	XIII	87	215—216

* Ar = o-$NO_2 \cdot C_6H_4$.

	Found (%)					Required (%)			
Compound	C	H	N	S	Formula	C	H	N	S
XI (*a*)	51·4	3·5	13·8	15·6	$C_{17}H_{14}N_4O_4S_2$	51·9	3·4	13·6	15·55
XIV	52·7	4·3	16·8	13·0	$C_{11}H_{11}N_3O_2S$	53·0	4·45	16·9	12·9
XV	61·8	4·2	13·1	10·2	$C_{16}H_{13}N_3O_2S$	61·7	4·2	13·5	10·3
XII	56·9	3·6	12·1	13·9	$C_{22}H_{16}N_4O_4S_2$	56·8	3·5	12·1	13·8
XVI	67·2	4·0	11·5	9·0	$C_{21}H_{15}N_3O_2S$	67·5	4·05	11·3	8·6
XIII	61·9	3·6	10·5	12·2	$C_{27}H_{18}N_4O_4S_2$	61·6	3·4	10·65	12·2

TABLE 4.

Products of hydrolysis of arylthiopyrazoles.

Starting materials (0·01 mole)	(o-$NO_2 \cdot C_6H_4 \cdot S)_2$ (%)	Pyrazole or arylthio-pyrazole (%)	Starting materials (0·01 mole)	(o-$NO_2 \cdot C_6H_4 \cdot S)_2$ (%)	Pyrazole or arylthio-pyrazole (%)
(XI)	—	57	(XIV)	13	39
(XII)	—	59	(XV)	11	51
(XIII)	—	64	(XVI)	9	57

*Di-*o*-nitrophenyl Disulphone.*—*o*-Nitrobenzenesulphinic acid[11] (5·6 g., 0·03 mole) was dissolved in glacial acetic acid (200 c.c.), and finely powdered potassium permanganate (1 g.)

was added. The mixture was shaken for 5 hr. and then the colour was discharged with sulphur dioxide. Water (10 c.c.) was added and the white precipitate filtered off and dried. Recrystallisation from acetone gave white needles of *di-*o*-nitrodiphenyl disulphone*, m. p. 185° (decomp.) (Found: C, 38·8; H, 2·1; N, 7·3; S, 17·1. $C_{12}H_8N_2O_8S_2$ requires C, 38·7; H, 2·15; N, 7·5; S, 17·2%).

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