409. *Derivatives of Sulphanilohydrazide.*

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In a search for new pest control agents, the following derivatives of sulphanilohydrazide have been prepared: hydrazones from aliphatic and aromatic aldehydes and ketones; cyclopentanone *N*-acylsulphanilohydrazones; and the *N*-alkoxycarbonyl derivatives.

Sulphonamides show activity towards a number of plant diseases.[1] In particular, sulphanilamide and the N^4-acyl derivatives exhibit systemic fungicidal activity against *Puccinia triticina* on wheat.[2] Accordingly, it was decided to prepare the sulphanilohydrazide derivatives listed in the annexed Tables, as potential pesticides. The methods used were standard and are indicated in the Experimental section.

N^4-Acetyl-*N'*-alkylidenesulphanilylhydrazides derived from aliphatic aldehydes were difficult to purify, often gave unsatisfactory analyses, and appeared to decompose slightly on repeated crystallisation.

Chromatography was of little value for characterisation of the products. However, a single ultraviolet absorption band at 260—262 mμ (ε 23,000—25,000) characterises N^4-acetylsulphanilohydrazide derivatives; the acetyl-free analogues have an additional, weaker, peak at 220—230 mμ.

Experimental

M. p.s were determined by using sealed tubes (to minimise decomposition).

N^4-Acetylsulphanilohydrazide has been assigned [3-5] m. p.s ranging from 176° to 198°, stated [4] to depend on the rate of heating. We found m. p. 188—190° (cf. Table 5). This compound was hydrolysed to sulphanilohydrazide by concentrated hydrochloric acid at 80—90° during 15 min. (cf. ref. 3).

Table 1. The arylidene derivatives were prepared by heating the hydrazide and aldehyde in ethanol, with or without sodium acetate. The primary alkylidene derivatives were obtained by Lehmann and Grivsky's method; [6] the best analytical figures were obtained for samples recrystallised rapidly and once only from ethanol.

Table 1.

N^4-Acetyl-*N'*-(primary alkylidene)- and -*N'*-arylidene-sulphanilohydrazides, *p*-NHAc·C_6H_4·SO_2·NH·N:CHR.

			Found (%)				Required (%)			
R	M. p.	Formula	C	H	N	S	C	H	N	S
H	84—86°	$C_9H_{11}N_3O_3S$	44·0	5·2	16·0	12·7	44·8	4·6	17·4	13·3
Pr^n	Amorphous	$C_{12}H_{17}N_3O_3S$	50·6	5·5	14·4	10·6	50·9	6·0	14·8	11·3
Pr^i	134—136	$C_{12}H_{17}N_3O_3S$	50·7	5·7	14·7	10·4	50·9	6·0	14·8	11·3
Ph	188—190 *	$C_{15}H_{15}N_3O_3S$	57·3	4·9	12·8	10·1	56·8	4·7	13·2	10·2
o-HO·C_6H_4	226—228	$C_{15}H_{15}N_3O_4S$	54·1	4·8	12·7	9·2	54·1	4·5	12·6	9·6
p-HO·C_6H_4	206—208	$C_{15}H_{15}N_3O_4S$	54·4	5·0	12·6	9·2	54·1	4·5	12·6	9·6
o-NO_2·C_6H_4	216—218	$C_{15}H_{14}N_4O_5S$	49·4	3·8	15·5	8·8	49·7	3·9	15·5	8·8
p-ClC_6H_4	210—211	$C_{15}H_{14}ClN_3O_3S$	50·8	4·1	12·4	9·2	51·2	4·0	11·95	9·1
2,4-$Cl_2C_6H_3$	229—230	$C_{15}H_{13}Cl_2N_3O_3S$ †	45·9	3·7	10·6	8·3	46·6	3·4	10·9	8·3
p-NMe_2·C_6H_4	220	$C_{17}H_{20}N_4O_3S$	56·8	5·7	16·2	8·2	56·7	5·55	15·55	8·9
Ph·CH:CH·CH	204—206	$C_{17}H_{17}N_3O_3S$	59·4	4·8	11·8	8·6	59·5	5·0	12·25	9·3

* Lit.,[3] 182°. † Found: Cl, 18·4. Reqd.: Cl, 18·4%.

Table 2. The ketone derivatives were prepared in the same way as those of aromatic aldehydes.

[1] Rudd-Jones, *Outlook on Agric.*, 1956, **1**, 111.
[2] Crowdy, Elias, and Rudd-Jones, *Ann. Appl. Biol.*, 1958, **46**, 149.
[3] Curtius and Stoll, *J. prakt. Chem.*, 1926, **112**, 117.
[4] Jensen and Hansen, *Acta Chem. Scand.*, 1952, **6**, 195.
[5] Roth and Degering, *J. Amer. Chem. Soc.*, 1945, **67**, 126; Niemiec, *ibid.*, 1948, **70**, 1068; Seppi, *Boll. Chim. farm.*, 1947, **86**, 178; Temmler, G.P. 874,443/1953.
[6] Lehmann and Grivsky, *Bull. Soc. chim. belges*, 1946, **55**, 52.

TABLE 2.

N^4-Acetyl-N'-(secondary alkylidene)- and -N'-cycloalkylidene-sulphanilohydrazides, *p*-NHAc·C_6H_4·SO_2·NH·N:CRR'.

R	R'	M. p.	Formula	Found (%) C	H	N	S	Required (%) C	H	N	S
Me	Me	190—192° *	$C_{11}H_{15}N_3O_3S$	48·5	5·8	15·7	—	49·0	5·6	15·6	—
Me	Et	181—182	$C_{12}H_{17}N_3O_3S$	50·9	6·0	14·8	11·1	50·9	6·0	14·8	11·3
Me	Bu^t	196—198	$C_{14}H_{21}N_3O_3S$	53·6	7·0	13·9	—	54·0	6·75	13·5	—
Me	$EtO_2C·CH_2$	160—162 †	$C_{14}H_{19}N_3O_5S$	49·1	5·6	9·0	—	49·3	5·6	9·4	—
Bu^n	Bu^n	170—172	$C_{17}H_{27}N_3O_3S$	57·5	7·6	11·8	9·1	57·8	7·65	11·9	9·1
Pr^i	Pr^i	194—196	$C_{15}H_{23}N_3O_3S$	55·4	7·2	13·4	10·0	55·4	7·1	12·9	9·8
Ph	Ph	220	$C_{21}H_{19}N_3O_3S$	63·9	5·2	10·4	8·6	64·1	4·8	10·7	8·1
Ph	Cyclohexyl	200—202	$C_{21}H_{25}N_3O_3S$	63·5	6·4	10·7	7·6	63·2	6·3	10·5	8·0
Me	*p*-HO·C_6H_4	212—213	$C_{16}H_{17}N_3O_4S$	54·7	4·5	12·3	8·8	55·3	4·9	12·1	9·2
Me	*p*-Br·C_6H_4	230—232	$C_{16}H_{16}BrN_3O_3S$	47·0	3·9	10·4	7·4	46·8	3·9	10·2	7·8
$-[CH_2]_4-$		198—199	$C_{13}H_{17}N_3O_3S$	53·2	5·7	14·9	10·8	52·9	5·8	14·2	10·9
$-[CH_2]_5-$		114—116	$C_{14}H_{19}N_3O_3S$	53·5	6·0	13·2	10·2	53·4	6·15	13·6	10·4
$-CHMe·[CH_2]_4-$		164—166	$C_{15}H_{21}N_3O_3S$	55·3	6·5	12·8	9·8	55·7	6·5	13·0	9·9
$-CH_2·CHMe·[CH_2]_3-$		118—120	$C_{15}H_{21}N_3O_3S$	55·1	6·4	12·6	9·6	55·7	6·5	13·0	9·9
$-CH(CO_2Et)·[CH_2]_4-$		220—222	$C_{17}H_{23}N_3O_5S$	53·2	5·5	11·0	9·1	53·55	6·0	11·0	8·4
$-[CH_2]_2·CHMe·[CH_2]_2-$		178—180	$C_{15}H_{21}N_3O_3S$	55·9	7·2	12·3	9·4	55·7	6·5	13·0	9·9
$-CHPr^i·[CH_2]_2·CHMe·CH_2-$		159—160	$C_{18}H_{27}N_3O_3S$	58·8	7·3	11·3	8·6	59·15	7·45	11·5	8·8
$-[CH_2]_6-$		185—187	$C_{15}H_{21}N_3O_3S$	55·3	6·7	13·0	9·8	55·7	6·5	13·0	9·9
$-CHMe·[CH_2]_5-$		172—174	$C_{16}H_{23}N_3O_3S$	56·3	7·2	11·8	9·2	56·95	6·9	12·45	9·5
$-CH(CO_2Et)·[CH_2]_3-$		200—202	$C_{16}H_{21}N_3O_5S$	51·9	5·9	12·0	8·5	52·3	5·7	11·4	8·7
$-CH(CN)·[CH_2]_3-$		180—182	$C_{14}H_{16}N_4O_3S$	53·0	4·7	16·8	—	52·5	5·0	17·5	—

* Curtius and Stoll,[3] record m. p. 172—174°.

† Rodionov and Fedovova (*Izest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1952, 1049) record m. p. 118—120°.

TABLE 3.

N^4-Acyl-N'-cyclopentylidenesulphanilohydrazides, *p*-R·CO·NH·C_6H_4·SO_2·NH·N:C<$[CH_2]_4$.

R	M. p.	Formula	Found (%) C	H	N	S	Required (%) C	H	N	S
Pr^i	182—183°	$C_{15}H_{21}N_3O_3S$	55·3	6·7	13·1	9·5	55·7	6·5	13·0	9·9
n-C_5H_{11}	181—182	$C_{17}H_{25}N_3O_3S$	57·5	6·6	12·4	9·2	58·1	7·1	11·9	9·1
n-$C_{11}H_{23}$	146—148	$C_{23}H_{37}N_3O_3S$	63·6	8·4	9·8	7·0	63·4	8·5	9·65	7·3
$Cl·CH_2·CH_2$	198—200	$C_{14}H_{18}ClN_3O_3S$	49·0	5·4	12·2	9·3	48·9	5·2	12·2	9·3
$EtS·CH_2$	109—111	$C_{15}H_{21}N_3O_3S_2$	50·2	6·3	11·6	17·4	50·7	5·9	11·8	18·0
Ph	216—218	$C_{18}H_{19}N_3O_3S$	60·3	5·3	12·1	8·9	60·5	5·3	11·8	9·0
Bu^n	176—178	$C_{16}H_{23}N_3O_3S$	55·8	6·0	12·8	9·1	56·95	6·9	12·45	9·5
n-C_6H_{13}	104—106	$C_{18}H_{27}N_3O_3S$	60·9	7·4	11·5	8·2	59·15	7·45	11·5	8·8
3,5-$(NO_2)_2C_6H_3$	216—218	$C_{18}H_{17}N_5O_7S$	47·7	3·5	15·3	7·2	48·3	3·8	15·7	7·2
2,4-$Cl_2C_6H_3$	186—188	$C_{18}H_{17}Cl_2N_3O_3S$ †	50·1	4·3	9·3	7·2	50·6	4·0	9·8	7·5

† Found: Cl, 16·0. Reqd.: Cl, 16·6%.

TABLE 4.

R	M. p.	Formula	Found (%) C	H	N	S	Required (%) C	H	N	S
(a) N^4-*Alkoxycarbonyl-N'-cyclopentylidenesulphanilohydrazides*, *p*-RO·CO·NH·C_6H_4·SO_2·NH·N:C<$[CH_2]_4$.										
Me	152—154°	$C_{13}H_{17}N_3O_4S$	50·5	6·0	13·3	10·0	50·2	5·5	13·5	10·3
Et	210—212	$C_{14}H_{19}N_3O_4S$	51·1	5·5	13·0	10·5	51·7	5·8	12·9	9·8
Bu^n	162—164	$C_{16}H_{23}N_3O_4S$	53·7	6·4	12·4	9·6	54·4	6·5	11·9	9·1
(b) N^4-*Acetyl-N'-alkoxycarbonylsulphanilohydrazides*, *p*-NHAc·C_6H_4·SO_2·NH·NH·CO_2R.										
Me	166—168	$C_{10}H_{13}N_3O_5S$	42·2	4·8	14·4	10·6	41·8	4·5	14·6	11·15
Et	160—162	$C_{11}H_{15}N_3O_5S$	44·3	5·5	13·9	10·0	43·85	5·0	13·95	10·6
Pr^n	163—166	$C_{12}H_{17}N_3O_5S$	47·1	5·8	12·8	9·7	45·7	5·4	13·3	10·2
Bu^n	104—108	$C_{13}H_{19}N_3O_5S$	46·6	5·9	13·1	9·7	47·4	5·8	12·8	9·7

Table 3. Cyclopentanone (12·8 g.) and sulphanilohydrazide (14·5 g.) were boiled in ethanol (140 c.c.) for 2 hr. Dissolution was complete in a few minutes. *N'-Cyclopentylidenesulphanilohydrazide* crystallised on cooling of the mixture; it recrystallised from ethanol as needles (13·5 g.) (see Table 5). The *cyclohexylidene derivative* was prepared analogously.

Treatment of the cyclopentanone hydrazone with the appropriate acyl chloride (1 equiv.) in pyridine and working up after 4—6 hr. gave the *compounds* listed in Table 3.

Table 4. Treatment of *N'*-cyclopentylidene- or N^4-acetyl-sulphanilohydrazide with an alkyl chloroformate and 1 equiv. of pyridine in benzene at 50—70° for 1 hr. gave the *compounds* listed in Table 4; they recrystallised from ethanol, ethanol–ether, or aqueous acetone.

TABLE 5.

Various sulphanilohydrazide derivatives, *p*-R·NH·C_6H_4·SO_2·NH·NR'R''.

					Found (%)				Required (%)			
R	R'	R''	M. p.	Formula	C	H	N	S	C	H	N	S
H	R'R'' = :C<[CH_2]$_4$		180—182°	$C_{11}H_{15}N_3O_2S$	51·8	6·0	16·2	12·8	52·2	5·9	16·6	12·6
H	RR' = :C<[CH_2]$_5$		175—177 *									
Ac	H	Ac	166—170 †	$C_{10}H_{13}N_3O_4S$	44·0	5·1	15·1	11·5	44·3	4·8	15·5	11·8
CO_2Et	H	CO_2Et	196—198	$C_{12}H_{17}N_3O_6S$	44·1	5·3	12·5	9·3	43·5	5·1	12·7	9·7
Ac	Me	Me	144—146	$C_{10}H_{15}N_3O_3S$	46·3	5·5	15·8	11·6	46·7	5·8	16·3	12·3
Ac	H	H	188—190	$C_8H_{11}N_3O_3S$	42·4	4·8	18·3	14·2	41·9	4·8	18·3	14·0
Pr^n·CO	H	H	141—143	$C_{10}H_{15}N_3O_3S$	47·1	6·2	15·9	12·6	46·7	5·8	16·3	12·3

* Temmler [5] gives m. p. 172°. † Niemiec [5] gives m. p. 191—192°.

Table 5. Sulphanilohydrazide and 2 mols. of ethyl chloroformate gave the N'N^4-*bisethoxycarbonyl derivative* recorded in Table 5.

p-Butyramidobenzenesulphonyl chloride (30 g.; m. p. 107—109°; obtained by the action of chlorosulphonic acid on butyranilide [7]), suspended in water (50 c.c.), was treated gradually, with stirring, with 90% hydrazine hydrate (10 ml.). The mixture was stirred overnight at room temperature, then cooled, and the N^4-*butyrylsulphanilohydrazide* that separated was collected, washed with ice–water, dried, and recrystallised twice from ethanol, forming needles (8·5 g.) (see Table 5).

p-Acetamidobenzenesulphonyl chloride (44 g.) was added gradually to phenylhydrazine (44 g.) in 50% v/v aqueous methanol (70 c.c.) at 0° and the suspension was stirred at room temperature overnight. The *N'*-phenyl derivative was then collected, washed with ice–water, dried, and recrystallised from ethanol, forming needles (20 g.), m. p. 160—161° (Roth and Degering [5] give m. p. 157—159°).

Use of *NN*-dimethylhydrazine similarly gave N^4-*acetyl*-N'N'-*dimethylsulphanilohydrazide* (see Table 5).

Chromatography. On paper chromatography in (i) butan-1-ol–acetic acid–water (4 : 1 : 5) or butan-1-ol–aqueous ammonia (*d* 0·88)–water (4 : 1 : 5), with a *p*-dimethylaminobenzaldehyde spray, the hydrazine derivatives gave orange ultraviolet-fluorescent spots, mainly close to the solvent front (R_F 0·92—0·97). In system (i), double spots (R_F 0·40, 0·90) were observed, probably owing to ionisation of the bases. With the isopentyl alcohol–collidine–water system used [8] for fatty acid hydrazides, the sulphanilohydrazides ran close to the solvent front.

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[7] Adams, Long, and Johanson, *J. Amer. Chem. Soc.*, 1939, **61**, 2342.
[8] Satake and Seki, *J. Chem. Soc. Japan*, 1950, **4**, 557.