The Action of Sodium Sulphide on 1,3,4-Oxadiazolium Salts

By G. V. Boyd * and A. J. H. Summers, Department of Chemistry, Chelsea College of Science and Technology, London S.W.3

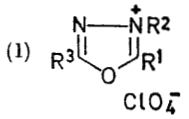
N-Aryl-1,3,4-oxadiazolium salts react with sodium sulphide to yield *N'*-acyl-*N*-aryl-*N*-thioacylhydrazines, which cyclise in the presence of acetic anhydride and perchloric acid to give 1,3,4-thiadiazolium perchlorates, the original oxadiazolium salts, or a mixture of the two, depending on the nature of the substituents. Oxadiazolo[3,2-*a*]-pyridinium salts similarly yield 1-acylaminopyridine-2-thiones, two of which have been converted into 1,3,4-thiadiazolo[3,2-*a*]pyridinium perchlorates.

1,3,4-OXADIAZOLIUM salts are highly susceptible to attack by nucleophilic reagents;[1] the initially formed oxadiazolines may undergo ring opening to yield derivatives of hydrazine, which, in turn, may cyclise to *s*-triazoles,[2] *s*-triazolium salts,[2] or pyrazoles.[3] We now describe the action of sodium sulphide on oxadiazolium salts and the behaviour of the products under strongly acidic conditions.

When triphenyloxadiazolium perchlorate (1a) was added to aqueous sodium sulphide a red solution resulted; acidification gave a yellow precipitate whose analytical figures and i.r. spectrum showed it to be a benzoylthiobenzoylphenylhydrazine (2a) or (3a). Analogous compounds were obtained from the salts (1b—f). The products are assigned structures (2) by analogy with other compounds formed from oxadiazolium salts: the reactions with sodium ethoxide,[1] amines,[2] and carbanions [3] are known to proceed *via* initial attack at C-2 of the oxadiazolium ring. In the present case the ions (4) would be formed, leading to compounds (2) rather than the isomers (3). This structural assignment is supported by two pieces of evidence: (*a*) compound (3b) is described in the literature [4] and is different from the product we obtained from the salt (1b); (*b*) the thioacylhydrazines prepared from the 2-phenyloxadiazolium salts (1a, d, and f) are deep yellow ($\lambda_{max.}$ 304 nm.), whereas the products from the 2-methyl salts (1b, c and e) are pale yellow ($\lambda_{max.}$ 275 or 284 nm.). This suggests that the former compounds all possess the thiobenzoylhydrazine chromophore (*cf.* thiobenzamide, $\lambda_{max.}$ 315 nm.)[5] and that the latter are thioacetyl derivatives (*cf.* *NN*-dimethylthioacetamide, $\lambda_{max.}$ 269 nm.),[5] in agreement with the structures (2a—f).

Successive treatment of the oxadiazolopyridinium salts (6a—c)[6] with sodium sulphide and hydrochloric acid gave the pyridine-2-thione derivatives (7a—c), all of which had $\lambda_{max.}$ 335 nm. Oxadiazolopyridinium salts without substituents in the pyridine ring did not yield identifiable products.

Since pyrylium [7] and 3-azapyrylium salts [8] can be transformed into thio-analogues *via* acyclic sulphur-containing intermediates, it was expected that the thioacylhydrazines would be converted into 1,3,4-thiadiazolium salts (5) in acidic media. We accordingly treated the triphenyl derivative (2a) with acetic anhydride–perchloric acid and obtained the thiadiazolium



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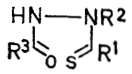

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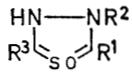

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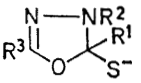

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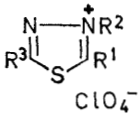
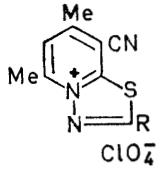


(5)

	R^1	R^2	R^3
a;	Ph	Ph	Ph
b;	Me	Ph	Ph
c;	Me	Ph	Me
d;	Ph	Ph	Me
e;	Me	*p*-$O_2N{\cdot}C_6H_4$	Me
f;	Ph	Ph	$PhCH_2$



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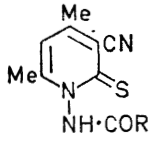
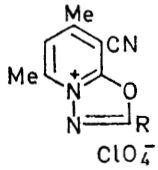


(7)

a; R = Me
b; R = Et
c; R = Ph



(6)

salt (5a) in 88% yield. Attempts to extend the synthesis to the other thioacylhydrazines yielded the following results. The thiobenzoyl compounds (2d and f) gave the thiadiazolium salts (5d and f); the thioacetylhydrazines (2b and c), on the other hand, afforded the original oxadiazolium salts. From the *N*-*p*-nitrophenyl derivative (2e) we obtained a 2 : 1 mixture of oxadiazolium (1e) and thiadiazolium (5e) perchlorates. The pyridinethiones (7a and b) gave thiadiazolopyridinium salts; compound (8a) was isolated in low yield and formation of the corresponding oxadiazolopyridinium salt cannot be ruled out. The benzamido-

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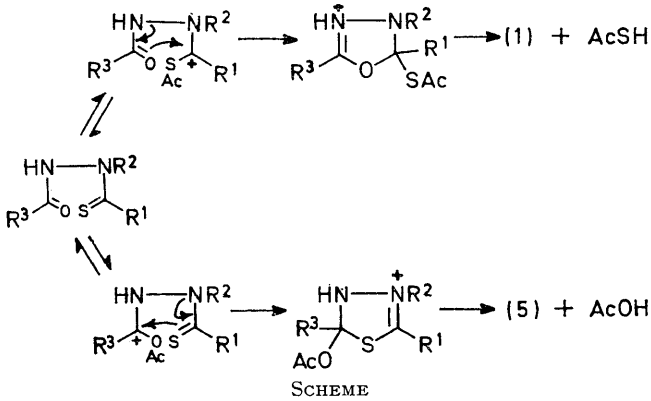
[2] G. V. Boyd and A. J. H. Summers, *J. Chem. Soc.* (*C*), 1971, 409.
[3] G. V. Boyd and S. R. Dando, *J. Chem. Soc.* (*C*), 1971, 225.
[4] G. Corsi, *Ann. Chim.* (*Italy*), 1966, **56**, 1203.
[5] A. Burawoy, *Ber.*, 1931, **64**, 481.
[6] G. V. Boyd and S. R. Dando, *J. Chem. Soc.* (*C*), 1970, 1397.
[7] R. Wizinger and P. Ulrich, *Helv. Chim. Acta*, 1956, **39**, 207.
[8] R. Schmidt, *Chem. Ber.*, 1969, **102**, 269.

derivative (7c) afforded an inseparable mixture which was shown by analysis and n.m.r. spectroscopy to contain equimolecular amounts of the thiadiazolopyridinium perchlorate (8c) and its oxygen analogue (6c).

The course of the cyclisation of acylthioacylhydrazines may be rationalised as follows. The first step is assumed to be attack by the acetylium ion on sulphur or oxygen; this is followed by cyclisation and loss of thioacetic acid or acetic acid, respectively (see Scheme). The direction of the initial attack thus determines the nature of the product. The electron-withdrawing effect of the phenyl group in thiobenzoyl compounds would favour acetylation on the oxygen atom and hence formation of thiadiazolium ions; whereas the electron-releasing methyl group in thioacetyl derivatives directs



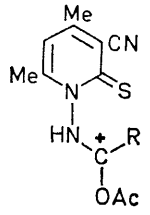
SCHEME

the acetylium ion to the sulphur atom so that oxadiazolium salts are produced. In the thioacetyl-*N*-nitrophenylhydrazine (2e) the electron-releasing effect of the methyl group may be balanced by the electron withdrawal by the *p*-nitrophenyl substituent; acetylation consequently occurs on both oxygen and sulphur atoms and ring-closure proceeds in both senses.

In the pyridine series the situation is less clear. Formation of the pyridinium ion (9) would appear to be favoured, and one might therefore expect only oxadiazolopyridinium salts to be formed, contrary to the experimental findings. It is possible that the stable ion (9) is not readily attacked by the weakly nucleophilic oxygen atom of the amide group, so that the small concentration of the alternative ion (10) present in the equilibrium mixture governs the course of the cyclisation. It is also conceivable, though less likely, that the presence of the cyano-substituent affects the reaction, but it was not possible to test this possibility because of our failure to prepare pyridine-2-thiones unsubstituted in the pyridine ring.

The *N*-arylthiadiazolium perchlorates decomposed slowly at room temperature, even when kept in a vacuum desiccator; * the bicyclic salts (8a and b) were much more stable. Several 1,3,4-thiadiazolium salts have been prepared by alkylation of thiadiazoles;[9] but the only simple *N*-arylthiadiazolium salt reported previously appears to be the chloride corresponding to compound (5a),[10] which was prepared by the action of hydrogen

(9)



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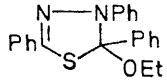

(11)

chloride on the ethoxythiadiazoline (11). Since the i.r. spectrum reported for the chloride differs in several respects from that of the perchlorate, we treated the latter with sodium ethoxide and obtained the ethoxy-derivative (11), thus establishing the identity of the cations in the two salts.

EXPERIMENTAL

Perchloric acid was of 70% strength. M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra refer to Nujol mulls. ^{1}H N.m.r. spectra were recorded for solutions in trifluoroacetic acid at 60 MHz with a Perkin-Elmer R10 spectrometer; u.v. spectra were determined for solutions in chloroform with a Perkin-Elmer 137 spectrophotometer. The preparation of 1,3,4-oxadiazolium and 1,3,4-oxadiazolo[3,2-*a*]pyridinium salts has been described.[6]

Acylthioacylarylhydrazines and N-Acylaminopyridine-2-thiones.—The oxadiazolium or oxadiazolopyridinium salt (4·0 g.) was added in small portions to a well stirred solution of sodium sulphide (4·0 g.) in water (30 ml.). If any solid remained, sufficient acetone was added to give a clear solution. Concentrated hydrochloric acid was then added (to pH 1) and the resulting precipitate was collected, washed with water, dried, and recrystallised from ethanol. The following compounds were obtained: N′-*benzoyl*-N-*phenyl*-N-*thiobenzoylhydrazine* (2a) (2·4 g., 80%), yellow needles, m.p. 192—193°, $\nu_{max.}$ 3230, 1665, and 1320 cm.$^{-1}$, $\lambda_{max.}$ 304 nm. (ε 10,000) (Found: C, 72·3; H, 4·8; N, 8·3; S, 9·0. $C_{20}H_{16}N_2OS$ requires C, 72·3; H, 4·9; N, 8·4; S, 9·6%); N′-*benzoyl*-N-*phenyl*-N-*thioacetylhydrazine* (2b) (2·0 g., 61%), pale yellow, m.p. 160—163°, $\nu_{max.}$ 3210, 1665, and 1275 cm.$^{-1}$, $\lambda_{max.}$ 284 nm. (ε 17,500) (Found: C, 66·6; H, 5·4; N, 10·3: $C_{15}H_{14}N_2OS$ requires C, 66·6; H, 5·3; N, 10·4%); N′-*acetyl*-N-*phenyl*-N-*thioacetylhydrazine* (2c) (2·0 g., 67%), pale yellow, m.p. 165—167°, $\nu_{max.}$ 3170, 1670, and 1275 cm.$^{-1}$, $\lambda_{max.}$ 284 nm. (ε 13,200) (Found: C, 57·8; H, 5·8; N, 13·5. $C_{10}H_{12}N_2OS$ requires C, 57·7; H, 5·8; N, 13·5%); N′-*acetyl*-N-*phenyl*-N-*thiobenzoylhydrazine* (2d) (2·4 g., 75%), deep yellow, m.p. 139—141°, $\nu_{max.}$ 3180, 1675, and 1250 cm.$^{-1}$, $\lambda_{max.}$ 304 nm. (ε 11,500) (Found: C, 67·0; H, 5·2; N, 10·4; S, 5·3. $C_{15}H_{14}N_2OS$

* Great difficulty was experienced in obtaining sulphur analyses for thiadiazolium perchlorates. The n.m.r. spectra of the salts (5b—f) showed that they were homogeneous; it is estimated that the presence of 1% of the oxygen analogues would have been detected since methyl and methylene protons in thiadiazolium and oxadiazolium salts resonate at different fields.

[9] M. Ohta, *J. Pharm. Soc. Japan*, 1953, **73**, 1127; B. Holmberg, *Arkiv Kemi*, 1955, **9**, 47; R. A. Olofson and J. M. Landesberg, *J. Amer. Chem. Soc.*, 1966, **85**, 4263.

[10] R. Huisgen, R. Grashey, M. Seidel, H. Knupfer, and R. Schmidt, *Annalen*, 1962, **658**, 169.

requires C, 66·6; H, 5·3; N, 10·4; S, 5·9%); N′-*acetyl*-N-p-*nitrophenyl*-N-*thioacetylhydrazine* (2e) (2·8 g., 90%), pale yellow, m.p. 168° (decomp.), $\nu_{max.}$ 3160, 1680, and 1270 cm.$^{-1}$, $\lambda_{max.}$ 275 nm. (ε 13,000) (Found: C, 46·8; H, 4·4; N, 16·4. $C_{10}H_{11}N_3O_3S$ requires C, 47·3; H, 4·4; N, 16·6%); N-*phenyl*-N′-*phenylacetyl*-N-*thiobenzoylhydrazine* (2f) (3·4 g., 98%), bright yellow, m.p. 163—165°, $\nu_{max.}$ 3220, 1680, and 1260 cm.$^{-1}$, $\lambda_{max.}$ 304 nm. (ε 12,000) (Found: C, 72·85; H, 5·35; N, 8·1; S, 9·25. $C_{21}H_{18}N_2OS$ requires C, 72·8; H, 5·25; N, 8·1; S, 9·2%); 1-*acetamido*-4,6-*dimethyl*-2-*thioxopyridine*-3-*carbonitrile* (7a) (1·5 g., 42%), yellow needles, m.p. 177° (decomp.), $\nu_{max.}$ 3140, 2230, 1650, and 1220 cm.$^{-1}$, $\lambda_{max.}$ 335 nm. (ε 9300) (Found: C, 54·5; H, 5·1; N, 19·2; S, 13·9. $C_{10}H_{11}N_3OS$ requires C, 54·3; H, 5·0; N, 19·0; S, 14·4%), 4,6-*dimethyl*-1-*propionamido*-2-*thioxopyridine*-3-*carbonitrile* (7b), (1·5 g., 48%), yellow needles, m.p. 173° (decomp.), $\nu_{max.}$ 3190, 2230, 1655, and 1220 cm.$^{-1}$, $\lambda_{max.}$ 335 nm. (ε 12,000) (Found: C, 56·0; H, 5·6; N, 17·8; S, 13·8. $C_{11}H_{13}N_3OS$ requires C, 56·1; H, 5·6; N, 17·85; S, 13·6%). 1-Benzamido-4,6-dimethyl-2-thioxopyridine-3-carbonitrile (7c) decomposed on attempted recrystallisation, and analytical figures for the crude solid were unsatisfactory. It had $\nu_{max.}$ 3220, 2220, and 1665 cm.$^{-1}$, $\lambda_{max.}$ 335 nm.

Action of Acetic Anhydride and Perchloric Acid on Acylthioacylhydrazines and Acylaminopyridinethiones.—Each hydrazine derivative (1·0 g.) was suspended in acetic anhydride (8 ml.) and perchloric acid (0·8 ml.) was added at such a rate that the temperature did not rise above 40°. The product usually crystallised; if it did not, ether was added and the resulting gum was triturated with fresh ether until it solidified.

The following thiadiazolium salts were obtained: 2,3,5-*triphenyl*-1,3,4-*thiadiazolium perchlorate* (5a) [from compound (2a)], (1·1 g., 88%), m.p. 214—217° (from acetic acid), $\nu_{max.}$ 1620, 1600, and 1100 cm.$^{-1}$ (Found: C, 58·2; H, 3·55; N, 6·6; S, 6·2. $C_{20}H_{15}ClN_2O_4S$ requires C, 57·9; H, 3·65; N, 6·75; S, 7·7%); 5-*methyl*-2,3-*diphenyl*-1,3,4-*thiadiazolium perchlorate* (5d) [from compound (2d)] (1·0 g., 77%), m.p. 163—166° (from acetonitrile–ether), $\nu_{max.}$ 1625, 1600, and 1100 cm.$^{-1}$, τ 2·1—2·5 (m, 2 × Ph) and 6·9 (s, 5-Me) (Found: C, 51·3; H, 3·9; N, 8·0; S, 8·5. $C_{15}H_{13}ClN_2O_4S$ requires C, 51·05; H, 3·7; N, 7·9; S, 9·1%); 5-*benzyl*-2,3-*diphenyl*-1,3,4-*thiadiazolium perchlorate* (5f) [from compound (2f)] (0·9 g., 75%), m.p. 161—163° (from acetonitrile–ether), $\nu_{max.}$ 1615, 1600, and 1100 cm.$^{-1}$, τ 2·2—2·6 (m, 3 × Ph) and 5·4 (s, CH_2) (Found: C, 58·9; H, 4·0; N, 6·6; S, 6·8. $C_{21}H_{17}ClN_2O_4S$ requires C, 58·8; H, 4·0; N, 6·6; S, 7·5%); 8-*cyano*-2,5,7-*trimethyl*-1,3,4-*thiadiazolo*[3,2-a]*pyridinium perchlorate* (8a) [from compound (7a)] (0·6 g., 44%), m.p. 202—204° (from acetic acid), $\nu_{max.}$ 2240, 1660, 1620, and 1100 cm.$^{-1}$, τ 2·15 (s, pyridine), 6·85 (s, Me), 6·92 (s, Me), and 7·08 (s, Me) (Found: C, 39·6; H, 3·4; N, 13·7; S, 10·4. $C_{10}H_{10}ClN_3O_4S$ requires C, 39·55; H, 3·3; N, 13·85; S, 10·55%); 8-*cyano*-2-*ethyl*-5,7-*dimethyl*-1,3,4-*thiadiazolo*[3,2-a]*pyridinium perchlorate* (8b) [from compound (7b)] (1·0 g., 74%), m.p. 173—175° (from acetic acid), $\nu_{max.}$ 2240, 1660sh, 1620, and 1100 cm.$^{-1}$ (Found: C, 41·8; H, 3·85; N, 13·4; S, 10·0. $C_{11}H_{12}ClN_3O_4S$ requires C, 41·55; H, 3·8; N, 13·2; S, 10·1%).

Treatment of the hydrazine derivative (2b) with acetic anhydride–perchloric acid yielded 2-methyl-3,5-diphenyloxadiazolium perchlorate (1b) (80%), identified by direct comparison (m.p., mixed m.p., and i.r. spectrum) with an authentic sample. Similarly, the oxadiazolium salt (1c) (67%) was obtained from compound (2c).

A suspension of the *p*-nitrophenylthioacetylhydrazine (2e) (0·8 g.) in acetic anhydride (5 ml.) was slowly treated with perchloric acid (0·4 ml.). Addition of ether to the resulting solution precipitated a solid which was dissolved in acetonitrile (10 ml.). The solution was treated with ether to incipient turbidity whereupon the oxadiazolium salt (1e) (0·6 g.) crystallised. The filtrate, with more ether, gave 2,5-*dimethyl*-3-p-*nitrophenyl*-1,3,4-*thiadiazolium perchlorate* (5e) (0·3 g.), m.p. 210° (decomp.), $\nu_{max.}$ 1625, 1595, 1455, and 1100 cm.$^{-1}$, τ 1·3 and 1·9 (d, *J* 9 Hz, Ar), 6·85 (s, 2-Me), and 7·18 (s, 5-Me) (Found: C, 35·7; H, 3·0; N, 12·6; S, 9·0. $C_{10}H_{10}ClN_3O_6S$ requires C, 35·8; H, 3·0; N, 12·5; S, 9·55%).

Treatment of the benzamidopyridine-2-thione (7c) (3·1 g.) with acetic anhydride (18 ml.) and perchloric acid (1·6 ml.) gave a precipitate (2·1 g.), m.p. 241—243°, shown to be a 1 : 1 mixture of the oxadiazolopyridinium salt (6c) and its sulphur analogue (8c) by its n.m.r. spectrum [τ 1·15—2·2 (m, pyridine and Ph), and 6·75, 6·85, 7·0, and 7·05 (four methyl singlets of equal intensity)] and analytical figures (Found: C, 50·4; H, 3·4; N, 11·7; S, 4·5. $C_{15}H_{12}ClN_3O_5$,-$C_{15}H_{12}ClN_3O_4S$ requires C, 50·4; H, 3·4; N, 11·75; S, 4·5).

5-*Ethoxy*-2,4,5-*triphenyl*-Δ²-1,3,4-*thiadiazoline* (11).—The triphenylthiadiazolium perchlorate (5a) (0·43 g.) was added to a solution of sodium ethoxide [from sodium (0·06 g.) and ethanol (15 ml.)]; the resulting solution deposited the thiadiazoline (0·35 g., 94%), m.p. 124—125° (lit.,[10] 128·5—129·5°), i.r. spectrum identical with that reported.[10]

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