Studies on Mesoionic Compounds. Part 11.[1] Alkylation of 5-Acylamino-1,2,3-thiadiazoles †

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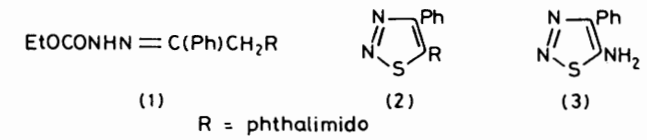
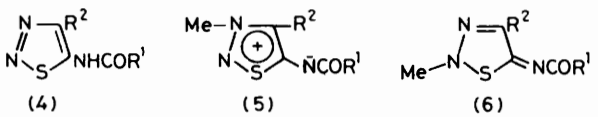
The alkylations of 5-acylamino-1,2,3-thiadiazoles (4) have been investigated; the N-3 position is preferably alkylated forming new mesoionic heterocycles (5) and (10). The mesoionic 1,2,3-thiadiazolium-5-alkoxy- and -5-aryloxy-carbonylaminides are converted into the corresponding salts of the 5-imine derivatives (11) by hydrolysis with hydrochloric acid.

In a previous paper [2] we reported the synthesis of new mesoionic 1,2,3-thiadiazolium-5-olate and -5-thiolate systems.[3] The latter could be converted into a novel class of mesoionic heterocycle, 1,2,3-thiadiazolium-5-methylaminides, by treatment with methyl iodide followed by methylamine. We also prepared 4-methoxy-1,2,3-thiadiazolium-5-ethoxycarbonylaminide from a 5-ethoxycarbonylamino-1,2,3-thiadiazolium-4-olate derivative.[4] However, these two procedures are not general methods for synthesis of the mesoionic 1,2,3-thiadiazolium-5-aminide system on account of, respectively, restriction on the amine and the structure of the original mesoionic compound. We have now investigated the alkylation of the 5-acylamino-1,2,3-thiadiazoles (4) which yields a new mesoionic system.[5]‡

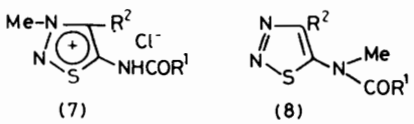


(1) (2) (3)

R = phthalimido



(4) (5) (6)



(7) (8)

a; R^1 = Ph, R^2 = H d; R^1 = OEt, R^2 = Ph
b; R^1 = OPh, R^2 = H e; R^1 = Me, R^2 = H
c; R^1 = OEt, R^2 = H f; R^1 = Me, R^2 = Ph

The starting compounds (4a—c) were prepared from diazomethane and acylisothiocyanates according to reported procedures.[6,7] Compound (4d) was obtained by ethoxycarbonylation of 5-amino-4-phenyl-1,2,3-thiadiazole (3) which was prepared by treatment of 2-phthalimidoacetophenone ethoxycarbonylhydrazone (1) with thionyl chloride [8] followed by cleavage of the phthalimido group with hydrazine. The reactions of compounds (4a and c) with dimethyl sulphate at elevated temperatures followed by alkali gave the monomethyl compounds (5a and c) as the sole products. The ^{1}H n.m.r. spectra of these products showed signals for the *N*-methyl group at δ 4.3 and for the ring protons at δ 8.5 (5a) and 8.25 (5c). These values are very similar to those of structurally similar mesoionic compounds, *e.g.* 3-methyl *N*-acylsydnone imines [9] and 3-methyl-2-phenyl-1,3-thiazolium-5-benzoylaminide.[10] The *N*-methyl and ring-proton signals of the hydrochlorides (7) were shifted downfield compared with the peaks shown by the free bases (5); this suggests that the ring current is affected by the protonation of the exocyclic hetero-atom. Furthermore, on comparison of the i.r. spectra the carbonyl stretching bands of the free bases (5) were at lower frequencies by *ca.* 100 cm^{-1} compared with those of the salts (7). This phenomenon has been found in the case of *N*-acylsydnone imines and their salts, and has been interpreted by considering polarisation of the carbonyl group.[9] The mass spectra of (5a) and (5c) showed a common fragment peak at *m/e* 42 which was attributed to Me–$\overset{+}{N}$≡CH. Nunn *et al.*[11] have reported that the quarternisation of benzo-1,2,3-thiadiazole with alkyl halide occurrs exclusively at N-3. On the basis of the above results, it is reasonable to presume the formulation of (5a and c) as mesoionic compounds.

The methylations of (4) with methyl fluorosulphonate, on the other hand, gave the mesoionic compounds (5) accompanied by the alternative methylated compounds (6). Although the i.r. spectra of (5) and (6) showed carbonyl stretching absorptions at almost exactly corresponding regions, in the n.m.r. spectra the *N*-methyl signals of (6) occurred at slightly higher field than those of (5). The mass spectra of these isomers (5) and (6), in spite of showing similar patterns to each other, showed clearly the structural differences. The fragment ions Me–$\overset{+}{N}$≡CR (R = H, *m/e* 42; R = Ph, *m/e* 118), as mentioned above, were observed in the spectra of (5). However, they were absent in the spectra of (6), but a common peak at *m/e* 61 which could be assigned to Me–$\overset{+}{N}$=S was detected in all spectra. Goerdeler and Gnad [7] have reported that alkylation of (4b) with trimethyloxonium tetrafluoroborate yielded an *N*-2-methylated compound. They excluded a mesoionic

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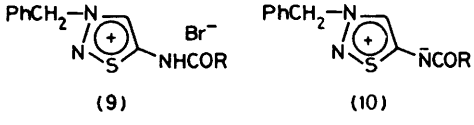
‡ In the course of this study, a similar preparation of a derivative of 1,2,3-thiadiazolium-5-methoxycarbonylaminide and its *X*-ray diffraction analysis have been reported (ref. 5).

structure for the product of this reaction on the basis of its solubility and melting point. We consider that their claim is incorrect because the physical data of the reported product are in agreement with those of compound (5b) [reported: m.p. 167 °C, $\lambda_{max.}$ (MeOH) 218 (log ε 4.19), 245 (4.10), and 337 nm (4.09); (5b): m.p. 167—169 °C, $\lambda_{max.}$ (MeOH) 217 (log ε 4.22), 245 (4.06), and 338 nm (4.04)].

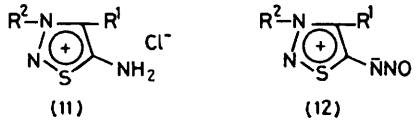
Whereas methylation of (4b and c) with diazomethane gave two products (5b and c) and (8b and c), the reaction of (4a) yielded (5a), (6a), and a trace of (8a). The structure of the last product was presumed from the spectral data [δ 3.7 (NMe), 7.65 (Ph), and 8.7 (4-H); $\nu_{max.}$ 1 650 cm^{-1} (CO)]. Thus, N-3 of the 1,2,3-thiadiazole (4) is very favourable to attack by alkylating agents. Heating of (4a and c) with benzyl bromide afforded 3-benzyl-1,2,3-thiadiazolium bromides (9a and b), which also gave the corresponding mesoionic compounds (10a and b) by treatment with alkali.

The above mesoionic compounds (5) and (10) were very



(9) (10)

a; R = Ph
b; R = OEt



(11) (12)

a; R^1 = H, R^2 = Me
b; R^1 = Ph, R^2 = Me
c; R^1 = H, R^2 = $PhCH_2$

stable to reduction (catalytic, lithium aluminium hydride and sodium borohydride), and did not undergo 1,3-dipolar cycloaddition and electrophilic substitution reactions [(5a—c) and (10)]. As they were also stable to acid and alkali, the acyl groups could not be hydrolysed under ordinary conditions. However, the hydrolysis of the ester groups of (5b—d) and (10b) was achieved by heating with concentrated hydrochloric acid in a sealed tube giving the salts of the 5-imine derivatives (11). These salts (11) were easily acetylated with acetic anhydride in the presence of pyridine to give the hydrochlorides (7e and f), which afforded the free bases (5e and f) by treatment with alkali. Direct treatment of the salts (11a and c) with alkali involved decomposition; similar treatment of (11b) gave 3-methyl-4-phenyl-1,2,3-thiadiazolium-5-aminide as an oil whose structure was confirmed by the n.m.r. and i.r. spectra and by acetylation to afford compound (5f).

The salts (11) afforded the *N*-nitroso-derivatives (12) in high yield on reaction with sodium nitrite in tetrafluoroboric acid. Attempts to convert the *N*-nitroso group of (12) into an exocyclic oxygen atom [12] were unsuccessful.

EXPERIMENTAL

General details are given in Part 6.[2]

2-Phthalimidoacetophenone Ethoxycarbonylhydrazone (1).—*N*-Phenacylphthalimide [13] (18.6 g), ethoxycarbonylhydrazine [14] (10.9 g), toluene-*p*-sulphonic acid (250 mg), and toluene (200 ml) were placed in a 500 ml round-bottomed flask equipped with a Dean–Stark water separator. The mixture was heated under reflux with stirring for 1.5 h. After cooling, the mixture was washed with water and dried (Na_2SO_4). Evaporation and recrystallisation of the residue from ethanol gave the *hydrazone* (1) (21.6 g, 88%) as needles, m.p. 164—166 °C (Found: C, 64.95; H, 4.9; N, 11.9. $C_{19}H_{17}N_3O_4$ requires C, 64.95; H, 4.9; N, 11.95%), $\nu_{max.}$ (KBr) 3 280 (NH) and 1 700 cm^{-1} (CO), δ($CDCl_3$) 1.43 (3 H, t, *J* 7 Hz, OCH_2Me), 4.4 (2 H, q, *J* 7 Hz, OCH_2Me), 4.92 (2 H, s, NCH_2), 7.2—8.2 (9 H, m, arom.), and 10.1 (1 H, s, NHCO).

4-Phenyl-5-phthalimido-1,2,3-thiadiazole (2).—Compound (1) (10.5 g) was added portionwise to ice-cooled thionyl chloride (20 ml) with stirring. The mixture was stirred at room temperature overnight. Evaporation and recrystallisation from ethyl acetate afforded the *phthalimidothiadiazole* (2) (8.5 g, 92%) as sticks, m.p. 164—166 °C (Found: C, 62.45; H, 3.2; N, 13.95. $C_{16}H_9N_3O_2S$ requires C, 62.55; H, 2.95; N, 13.65%), $\nu_{max.}$ (KBr) 1 710 cm^{-1} (CO), δ($CDCl_3$) 7.25—8.2 (s + m, arom.), *m/e* 307 (M^+).

5-Amino-4-phenyl-1,2,3-thiadiazole (3).—A solution of 80% hydrazine hydrate (2.25 g) in ethanol (30 ml) was added slowly to the phthalimido-derivative (2) (9.2 g) in boiling ethanol (150 ml). After cooling, the precipitate was filtered off. The filtrate was concentrated, and the residue was chromatographed on alumina (basic, 30 g). Elution with chloroform gave a crystalline solid, which was recrystallised from benzene to give *5-amino-4-phenyl-1,2,3-thiadiazole* (3) (4.2 g, 79%) as leaflets, m.p. 142—145 °C (Found: C, 53.95; H, 3.7; N, 23.9. $C_8H_7N_3S$ requires C, 54.2; H, 4.0; N, 23.7%), $\nu_{max.}$ (KBr) 3 430 and 3 280 cm^{-1} (NH_2).

5-Ethoxycarbonylamino-4-phenyl-1,2,3-thiadiazole (4d).—A solution of ethyl chloroformate (6.2 g) in pyridine (20 ml) was added to a cooled solution of the amino-compound (3) (3.54 g) in pyridine (20 ml) with stirring. After 4 h, the mixture was diluted with water and extracted with chloroform. Evaporation gave an oil, which was stirred with a solution of ethanol (50 ml) and 5% sodium hydroxide (50 ml) at room temperature. After the formation of a clear solution, the mixture was acidified with 10% hydrochloric acid and extracted with chloroform. Usual work-up of the extract afforded the *urethane* (4d) (4.38 g, 88%) as needles, m.p. 125—126 °C (from cyclohexane) (Found: C, 52.8; H, 4.7; N, 16.65. $C_{11}H_{11}N_3O_2S$ requires C, 53.0; H, 4.45; N, 16.85%), $\nu_{max.}$ (KBr) 3 230 (NH) and 1 700 cm^{-1} (CO), δ($CDCl_3$) 1.35 (3 H, t, *J* 7 Hz, OCH_2Me), 4.4 (2 H, q, *J* 7 Hz, OCH_2Me), 7.65 (5 H, m, Ph), and 7.95br (1 H, s, CONH).

Methylation of (4) *with Dimethyl Sulphate.*—(*a*) A mixture of 5-benzoylamino-1,2,3-thiadiazole [6] (4a) (2 g) and dimethyl sulphate (2.4 g) in dimethylformamide (20 ml) was heated in a sealed tube at 170 °C for 1.5 h. After cooling, the mixture was diluted with water, neutralised with potassium carbonate, and extracted with chloroform. The extract was worked up as usual to give *3-methyl-1,2,3-thiadiazolium-5-benzoylaminide* (5a) (1.39 g, 65%) as leaflets, m.p. 190—191 °C (from isopropyl alcohol) (Found: C, 54.8; H, 3.9; N, 19.25. $C_{10}H_9N_3OS$ requires C, 54.8;

H, 4.15; N, 19.15%), $\nu_{max.}$ (KBr) 1 540 cm^{-1} (CO), $\lambda_{max.}$ (EtOH) 273 (log ε 3.98) and 347 nm (4.20), δ($CDCl_3$) 4.3 (3 H, s, NMe), 7.2—7.6 (3 H, m, arom.), 8.1—8.35 (2 H, m, arom.), and 8.5 (1 H, s, 4-H), *m/e* 219 (M^+), 204, 173, 105 (base peak), 77, and 42.

(*b*) Similarly, 5-ethoxycarbonylamino-1,2,3-thiadiazole [6] (4c) (500 mg), dimethyl sulphate (730 mg), and dimethylformamide (5 ml) were heated at 100 °C for 2 h. Addition of 10% potassium carbonate solution, extraction with chloroform, and usual work-up of the extract gave 3-*methyl*-1,2,3-*thiadiazolium-5-ethoxycarbonylaminide* (5c) (362 mg, 67%) as needles, m.p. 195—198.5 °C (from benzene) (Found: C, 38.3; H, 4.95; N, 22.4. $C_6H_9N_3O_2S$ requires C, 38.5; H, 4.85; N, 22.45%), $\nu_{max.}$ (KBr) 1 600 cm^{-1} (CO), δ($CDCl_3$) 1.3 (3 H, t, *J* 7 Hz, OCH_2*Me*), 4.2 (2 H, q, *J* 7 Hz, OCH_2Me), 4.3 (3 H, s, NMe), and 8.25 (1 H, s, 4-H), *m/e* 187 (M^+), 142, 117, 115 (base peak), 63, 46, and 42.

Methylation of (4) *with Methyl Fluorosulphonate*.—(*a*) A mixture of (4a) (410 mg) and methyl fluorosulphonate (3 ml) was stirred at room temperature for 1.5 h. Evaporation gave a crystalline solid, which was then treated with saturated sodium hydrogen carbonate solution and extracted with chloroform. Usual work-up of the extract afforded crystals, which were recrystallised from isopropyl alcohol to give the 3-*methyl compound* (5a) (221 mg, 50.5%) as needles, m.p. 189—191 °C, identical with an authentic sample.

The mother-liquor was concentrated and the residue was recrystallised from hexane to give 5-*benzoylimino*-2-*methyl*-Δ³-1,2,3-*thiadiazoline* (6a) (21 mg, 5%) as needles, m.p. 148—150 °C (Found: C, 54.6; H, 4.4; N, 19.4. $C_{10}H_9N_3OS$ requires C, 54.8; H, 4.15; N, 19.15%), $\nu_{max.}$ (KBr) 1 530 cm^{-1} (CO), δ($CDCl_3$) 4.1 (3 H, s, NMe), 7.4—7.7 (3 H, m, arom.), 8.25—8.6 (2 H, m, arom.), and 8.5 (1 H, s, 4-H), *m/e* 219 (M^+), 142, 105 (base peak), 77, 61, and 51.

(*b*) Similarly, 5-phenoxycarbonylamino-1,2,3-thiadiazole [7] (4b) (442 mg) and methyl fluorosulphonate (3 ml) were stirred at room temperature for 24 h. Work-up as above gave the products (5b) and (6b). 3-*Methyl*-1,2,3-*thiadiazolium-5-phenoxycarbonylaminide* (5b) (316 mg, 67%) as pale yellow needles, m.p. 167—169 °C (from benzene) (Found: C, 50.8; H, 3.8; N, 18.1. $C_{10}H_9N_3O_2S$ requires C, 51.05; H, 3.85; N, 17.85%), $\nu_{max.}$ (KBr) 1 600 cm^{-1} (CO), $\lambda_{max.}$ (MeOH) 217 (log ε 4.22), 245 (4.06) and 338 nm (4.04), δ($CDCl_3$) 4.4 (3 H, s, NMe), 7.35 (5 H, s, Ph), and 8.3 (1 H, s, 4-H), *m/e* 235 (M^+), 142 (base peak), 94, 77, 46, and 42; 2-*methyl*-5-*phenoxycarbonylimino*-Δ³-1,2,3-*thiadiazoline* (6b) (76 mg, 16%) as needles, m.p. 85—87 °C (from cyclohexane) (Found: C, 51.15; H, 4.05; N, 17.6. $C_{10}H_9N_3O_2S$ requires C, 51.05; H, 3.85; N, 17.85%), $\nu_{max.}$ (KBr) 1 580 cm^{-1} (CO), δ($CDCl_3$) 4.05 (3 H, s, NMe), 7.1—7.7 (5 H, m, Ph), and 8.15 (1 H, s, 4-H), *m/e* 235 (M^+), 142 (base peak), 86, 77, 61, and 43.

(*c*) Similar treatment of (4c) (519 mg) with methyl fluorosulphonate (2 ml) (30 min) and work-up as above yielded the products (5c) and (6c). 3-*Methyl*-1,2,3-*thiadiazolium-5-ethoxycarbonylaminide* (5c) (413 mg, 73.6%) as needles, m.p. 195—198 °C (from benzene), identical with the authentic sample; 5-*ethoxycarbonylimino*-2-*methyl*-Δ³-1,2,3-*thiadiazoline* (6c) (35 mg, 6%) was obtained as needles, m.p. 86—87 °C (from hexane) (Found: C, 38.5; H, 5.0; N, 22.2. $C_6H_9N_3O_2S$ requires C, 38.5; H, 4.85; N, 22.45%), $\nu_{max.}$ (KBr) 1 595 cm^{-1} (CO), δ($CDCl_3$) 1.3 (3 H, t, *J* 7 Hz, OCH_2*Me*), 4.0 (3 H, s, NMe), 4.35 (2 H, q, *J* 7 Hz, OCH_2Me), and 8.05 (1 H, s, 4-H), *m/e* 187 (M^+), 142, 115, 61, 43, 32, and 29 (base peak).

(*d*) A mixture of (4d) (2.49 g) and methyl fluorosulphonate 1.71 g) in chloroform (20 ml) was refluxed for 3 h. Concentration gave an oil, which was stirred with saturated sodium hydrogen carbonate solution and extracted with chloroform. Evaporation and recrystallisation from benzene afforded 3-*methyl*-4-*phenyl*-1,2,3-*thiadiazolium*-5-*ethoxycarbonylaminide* (5d) (1.54 g) as yellow needles, m.p. 151—153 °C (Found: C, 54.5; H, 4.95; N, 15.75. $C_{12}H_{13}N_3O_2S$ requires C, 54.75; H, 5.0; N, 15.95%), $\nu_{max.}$ (KBr) 1 580 cm^{-1} (CO), δ($CDCl_3$) 1.3 (3 H, t, *J* 7 Hz, OCH_2-*Me*), 4.2 (3 H, s, NMe), 4.25 (2 H, q, *J* 7 Hz, OCH_2Me), and 7.55 (5 H, s, Ph), *m/e* 263 (M^+), 218, 191 (base peak), 118, 77, and 63.

The mother-liquor was evaporated and the residue was chromatographed on silica gel (10 g). Elution with benzene gave 5-*ethoxycarbonylimino*-2-*methyl*-4-*phenyl*-Δ³-1,2,3-*thiadiazoline* (6d) (348 mg, 13%) as pale yellow needles, m.p. 124—126 °C (from hexane) (Found: C, 54.45; H, 5.0; N, 16.1. $C_{12}H_{13}N_3O_2S$ requires C, 54.75; H, 5.0; N, 15.95%), $\nu_{max.}$ (KBr) 1 590 cm^{-1} (CO), δ($CDCl_3$) 1.4 (3 H, t, *J* 7 Hz, OCH_2*Me*), 4.0 (3 H, s, NMe), 4.4 (2 H, q, *J* 7 Hz, OCH_2Me), 7.25—7.7 (3 H, m, arom.), and 8.25—8.6 (2 H, m, arom.), *m/e* 263 (M^+, base peak), 218, 191, 158, 148, 131, 121, 104, 77, and 61.

Further elution with chloroform gave an additional compound (5d) (420 mg, total yield 74%).

3-*Methyl*-5-*acylamino*-1,2,3-*thiadiazolium Chlorides* (7).—(*a*) A solution of (5a) (660 mg) in chloroform (5 ml) was cooled in an ice-bath and saturated with hydrogen chloride. The mixture was diluted with ether, and the precipitate was filtered off to afford 5-*benzoylamino*-3-*methyl*-1,2,3-*thiadiazolium chloride* (7a) (550 mg, 71%), m.p. 240 °C (decomp.) (Found: C, 46.65; H, 3.75; N, 16.7. $C_{10}H_{10}ClN_3OS$ requires C, 46.95; H, 3.95; N, 16.45%), $\nu_{max.}$ (KBr) 1 640 cm^{-1} (CO), δ(CD_3OD) 4.7 (3 H, s, NMe), 7.5—7.8 (3 H, m, arom.), 8.2—8.5 (2 H, m, arom.), and 10.1 (1 H, s, 4-H).

(*b*) A cooled solution of the compounds (5b—d) in methanol was saturated with hydrogen chloride. Concentration and recrystallisation of the residue gave the salts (7b—d). 3-*Methyl*-5-*phenoxycarbonylamino*-1,2,3-*thiadiazolium chloride* (7b) (88%) was obtained as needles, m.p. 148—151 °C (decomp.) (from isopropyl alcohol) (Found: C, 43.95; H, 3.7; N, 15.4. $C_{10}H_{10}ClN_3O_2S$ requires C, 44.2; H, 3.7; N, 15.45%), $\nu_{max.}$ (KBr) 1 680 cm^{-1} (CO), δ(CD_3OD) 4.75 (3 H, s, NMe), 7.2—7.6 (5 H, m, Ph), and 10.0 (1 H, s, 4-H); 5-*ethoxycarbonylamino*-3-*methyl*-1,2,3-*thiadiazolium chloride* (7c) (69%), needles, m.p. 156—159 °C (decomp.) (from acetone) (Found: C, 32.15; H, 4.5; N, 18.55. $C_6H_{10}ClN_3O_2S$ requires C, 32.2; H, 4.5; N, 18.8%), $\nu_{max.}$ (KBr) 1 690 cm^{-1} (CO), δ(CD_3OD) 1.4 (3 H, t, *J* 7 Hz, OCH_2*Me*), 4.5 (2 H, q, *J* 7 Hz, OCH_2Me), 4.6 (3 H, s, NMe), and 9.3 (1 H, s, 4-H); 5-ethoxycarbonylamino-3-methyl-4-phenyl-1,2,3-thiadiazolium chloride (7d) (quantitative), an oil, $\nu_{max.}$ (film) 1 690 cm^{-1} (CO), δ(CD_3OD) 1.35 (3 H, t, *J* 7 Hz, OCH_2*Me*), 4.35 (3 H, s, NMe), 4.45 (2 H, q, *J* 7 Hz, OCH_2Me), and 7.7 (5 H, s, Ph).

Methylation of (4) *with Diazomethane*.—(*a*) Ethereal diazomethane [from *N*-nitrosomethylurea (3 g), 50% potassium hydroxide (8 ml), and ether (30 ml)] was added to a suspension of (4a) (615 mg) in methanol (15 ml). The mixture was allowed to stand at room temperature for 4 h. After evaporation, the residue was recrystallised from

isopropyl alcohol to give the 3-methyl compound (5a) (352 mg, 53.5%) as needles, m.p. 189—191 °C. The mother-liquor was concentrated, and the residue was dissolved in hot hexane and filtered. From the filtrate the 2-methyl compound (6a) (223 mg, 34%), needles, m.p. 147—150 °C, was obtained. These products were identical with authentic samples.

The insoluble part in hexane (12 mg) contained the 5-(*N*-benzoylmethylamino)-compound (8a).

(*b*) Similar treatment of (4b) (221 mg) in acetone (30 ml) with an excess of diazomethane (1 h) yielded crystalline products, which were chromatographed on silica gel (2 g). Elution with benzene afforded 5-(*N*-phenoxycarbonylmethylamino)-1,2,3-thiadiazole (8b) (174 mg, 74%) as needles, m.p. 170—171 °C (from CCl_4) (lit.,[7] 168 °C), $\nu_{max.}$ (KBr) 1 710 cm^{-1} (CO), $\delta(CDCl_3)$ 3.8 (3 H, s, NMe), 7.15—7.7 (5 H, m, Ph), and 8.55 (1 H, s, 4-H).

Further elution with chloroform gave the 3-methyl compound (5b) (46 mg, 15%), m.p. 165—168 °C (from benzene), identical with an authentic sample.

(*c*) Similarly, compound (4c) (519 mg) in methanol (20 ml) was treated with an excess of diazomethane (24 h). Evaporation gave a crystalline residue, which was then heated with isopropyl ether and filtered. The filtrate was concentrated and recrystallised from cyclohexane to afford 5-(*N-ethoxycarbonylmethylamino*)-1,2,3-*thiadiazole* (8c) (350 mg, 62%) as needles, m.p. 76—77 °C (Found: C, 38.6; H, 4.7; N, 22.2. $C_6H_9N_3O_2S$ requires C, 38.5; H, 4.85; N, 22.45%), $\nu_{max.}$ (KBr) 1 695 cm^{-1} (CO), $\delta(CDCl_3)$ 1.4 (3 H, t, *J* 7 Hz, OCH_2Me), 3.55 (3 H, s, NMe), 4.4 (2 H, q, *J* 7 Hz, OCH_2Me), and 8.25 (1 H, s, 4-H).

From the insoluble part in hot isopropyl ether the 3-methyl compound (5c) (126 mg, 22%) was obtained as needles, m.p. 192—195 °C (from benzene), identical with an authentic sample.

Reaction of (4) *with Benzyl Bromide*.—(a) A mixture of (4a) (2 g) and benzyl bromide (1.7 g) in dimethylformamide (20 ml) was heated at 140 °C for 3.5 h. After cooling, the precipitate was filtered off and washed with ethanol to afford 5-*benzoylamino*-3-*benzyl*-1,2,3-*thiadiazolium bromide* (9a) (1.78 g, 48.5%), m.p. 230—235 °C (decomp.) (Found: C, 51.05; H, 3.75; N, 11.25. $C_{16}H_{14}BrN_3OS$ requires C, 51.05; H, 3.75; N, 11.15%), $\nu_{max.}$ (KBr) 1 630 cm^{-1} (CO), $\delta[(CD_3)_2SO]$ 6.15 (2 H, s, $PhCH_2$), 7.1—8.4 (10 H, m, 2 × Ph), and 9.55 (1 H, s, 4-H).

The salt (9a) (730 mg) and 5% sodium hydroxide (5 ml) were stirred at room temperature for 10 min. Extraction with chloroform and usual work-up of the extract gave 3-*benzyl*-1,2,3-*thiadiazolium*-5-*benzoylaminide* (10a) (470 mg, 82.5%), needles, m.p. 147—148 °C (from chloroform–ether) (Found: C, 65.15; H, 4.65; N, 14.4. $C_{16}H_{13}N_3OS$ requires C, 65.05; H, 4.45; N, 14.25%), $\nu_{max.}$ (KBr) 1 540 cm^{-1} (CO), $\lambda_{max.}$ (EtOH) 274 (log ε 4.08) and 349 nm (4.23), $\delta(CDCl_3)$ 5.6 (2 H, s, $PhCH_2$), 7.2—7.5 (3 H, m, arom.), 7.3 (5 H, s, Ph), 8.0—8.3 (2 H, m, arom.), and 8.35 (1 H, s, 4-H), *m/e* 295 (M^+), 204, 128, 105 (base peak), 91, 77, 65, and 51.

(b) A mixture of (4c) (1.73 g), benzyl bromide (5 ml), and toluene (5 ml) was heated at 100 °C for 1 h. Dilution with ether, filtration of the precipitate, and recrystallisation from acetone gave 3-*benzyl*-5-*ethoxycarbonylamino*-1,2,3-*thiadiazolium bromide* (9b) (3.25 g, 94%) as needles, m.p. 154—156 °C (decomp.) (Found: C, 42.05; H, 4.3; N, 12.1. $C_{12}H_{14}BrN_3O_2S$ requires C, 41.85; H, 4.1; N, 12.2%), $\nu_{max.}$ (KBr) 1 685 cm^{-1} (CO), $\delta(CD_3OD)$ 1.4 (3 H, t, *J* 7 Hz, OCH_2Me), 4.5 (2 H, q, *J* 7 Hz, OCH_2Me), 6.2 (2 H, s, $PhCH_2$), 7.35—7.9 (5 H, m, Ph), and 10.0 (1 H, s, 4-H).

The salt (9b) (1.65 g) was stirred with saturated sodium hydrogen carbonate solution (10 ml) at room temperature for 15 min. Extraction with chloroform and usual work-up of the extract afforded 3-*benzyl*-1,2,3-*thiadiazolium*-5-*ethoxycarbonylaminide* (10b) (1.2 g, 95%) as needles, m.p. 148—149 °C (from benzene) (Found: C, 54.45; H, 5.15; N, 15.75. $C_{12}H_{13}N_3O_2S$ requires C, 54.75; H, 5.0; N, 15.95%), $\nu_{max.}$ (KBr) 1 600 cm^{-1} (CO), $\delta(CDCl_3)$ 1.35 (3 H, t, *J* 7 Hz, OCH_2Me), 4.3 (2 H, q, *J* 7 Hz, OCH_2Me), 5.65 (2 H, s, $PhCH_2$), 7.5 (5 H, s, Ph), and 8.25 (1 H, s, 4-H), *m/e* 263 (M^+), 217, 191, 172, 91 (base peak), 65, 63, and 51.

3-*Alkyl*-5-*amino*-1,2,3-*thiadiazolium Chlorides* (11).—The compounds (5b—d) and (10b) were dissolved in concentrated hydrochloric acid (10 × volume of the ester), and the mixtures were heated in a sealed tube at 120—130 °C for 4.5—15 h. Concentration and recrystallisation of the residue from isopropyl alcohol gave the salts (11). Both of the esters (5b) and (5c) yielded 5-*amino*-3-*methyl*-1,2,3-*thiadiazolium chloride* (11a) in 67 and 85% yield, respectively; needles, m.p. 184—186 °C (decomp.) (Found: C, 23.85; H, 4.1; N, 27.55. $C_3H_6ClN_3S$ requires C, 23.75; H, 4.0; N, 27.7%), $\nu_{max.}$ (KBr) 1 580 cm^{-1} (C=N), $\delta(CD_3OD)$ 4.8 (3 H, s, NMe) and 8.8 (1 H, s, 4-H), *m/e* 115 (*M* − HCl) and 42 (base peak); 5-*amino*-3-*methyl*-4-*phenyl*-1,2,3-*thiadiazolium chloride* (11b) [64% from (5d)] had m.p. 221—223 °C (decomp.) (Found: C, 47.2; H, 4.4; N, 18.2. $C_9H_{10}ClN_3S$ requires C, 47.45; H, 4.45; N, 18.45%), $\nu_{max.}$ (KBr) 1 590 cm^{-1} (C=N), $\delta(CD_3OD)$ 4.25 (3 H, s, NMe) and 7.75 (5 H, s, Ph), *m/e* 191 (*M* − HCl) and 118 (base peak); 5-*amino*-3-*benzyl*-1,2,3-*thiadiazolium chloride* (11c) [85% from (10b)], sticks, had m.p. 193—194 °C (decomp.) (Found: C, 47.25; H, 4.55; N, 18.45. $C_9H_{10}ClN_3S$ requires C, 47.45; H, 4.45; N, 18.45%), $\nu_{max.}$ (KBr) 1 585 cm^{-1} (C=N), $\delta(CD_3OD)$ 5.95 (2 H, s, $PhCH_2$), 7.6 (5 H, s, Ph), and 8.9 (1 H, s, 4-H), *m/e* 191 (*M* − HCl) and 91 (base peak).

Acetylation of (11).—(*a*) A mixture of (11a) (303 mg), acetic anhydride (1 ml), and pyridine (0.2 ml) was stirred at room temperature for 6 h. Concentration and recrystallisation from isopropyl alcohol gave 5-*acetamino*-3-*methyl*-1,2,3-*thiadiazolium chloride* (7e) (303 mg, 78%) as plates, m.p. 232 °C (decomp.) (Found: C, 31.05; H, 4.15; N, 21.45. $C_5H_8ClN_3OS$ requires C, 31.0; H, 4.15; N, 21.7%), $\nu_{max.}$ (KBr) 1 660 cm^{-1} (CO), $\delta(CD_3OD)$ 2.5 (3 H, s, COMe), 4.7 (3 H, s, NMe), and 9.85 (1 H, s, 4-H). The salt (7e) (100 mg) was stirred with saturated sodium hydrogen carbonate solution (2 ml) at room temperature for 15 min. Extraction with chloroform and usual work-up of the extract gave 3-*methyl*-1,2,3-*thiadiazolium*-5-*acetylaminide* (5e) (79 mg, 97%) as needles, m.p. 135—136 °C (from benzene) (Found: C, 38.0; H, 4.6; N, 26.45. $C_5H_7N_3OS$ requires C, 38.2; H, 4.5; N, 26.75%), $\nu_{max.}$ (KBr) 1 560 cm^{-1} (CO), $\delta(CDCl_3)$ 2.4 (3 H, s, COMe), 4.4 (3 H, s, NMe), and 8.4 (1 H, s, 4-H), *m/e* 157 (M^+), 142, 115, 43 (base peak), 42, and 29.

(*b*) Similar treatment of (11b) (114 mg) with acetic anhydride (0.5 ml) and pyridine (0.1 ml) gave 5-*acetamino*-3-*methyl*-4-*phenyl*-1,2,3-*thiadiazolium chloride* (7f) (quantitative), $\nu_{max.}$ (Nujol) 1 680 cm^{-1} (CO), $\delta(CD_3OD)$ 2.45 (3 H, s, COMe), 4.45 (3 H, s, NMe), and 7.85 (5 H, s, Ph). The compound (7f) was treated with sodium hydrogen carbonate and worked up as above to afford 3-*methyl*-4-*phenyl*-1,2,3-*thiadiazolium*-5-*acetylaminide* (5f) (92 mg, 79%) as pale yellow needles, m.p. 207—208 °C (from benzene) (Found:

C, 56.9; H, 4.85; N, 17.9. $C_{11}H_{11}N_3OS$ requires C, 56.65; H, 4.75; N, 18.0%), $\nu_{max.}$ (KBr) 1 550 cm^{-1} (CO), $\delta(CDCl_3)$ 2.4 (3 H, s, COMe), 4.25 (3 H, s, NMe), and 7.6 (5 H, s, Ph).

This compound (5f) was also obtained in 59% yield by treatment of (11b) with sodium hydrogen carbonate, extraction with chloroform, followed by acetylation as above.

3-*Alkyl*-1,2,3-*thiadiazolium*-5-*nitrosoaminides* (12).—To a cooled mixture of the salts (11) in 10% tetrafluoroboric acid was added sodium nitrite (1 mol. equiv.) in the minimum amount of water. After stirring for 0.5—1 h, the yellow precipitate was filtered off and washed with water to give the *N*-nitroso-compounds (12). 3-*Methyl*-1,2,3-*thiadiazolium*-5-*nitrosoaminide* (12a) (89%), yellow needles, had m.p. 174—175 °C (from benzene) (Found: C, 25.2; H, 3.0; N, 38.75. $C_3H_4N_4OS$ requires C, 25.0; H, 2.8; N, 38.85%), $\nu_{max.}$ (KBr) 1 500 cm^{-1} (NNO), $\delta(CDCl_3)$ 4.6 (3 H, s, NMe) and 9.4 (1 H, s, 4-H); 3-*methyl*-4-*phenyl*-1,2,3-*thiadiazolium*-5-*nitrosoaminide* (12b) (88.5%), yellow needles, had m.p. 167—168 °C (from benzene) (Found: C, 48.8; H, 3.7; N, 25.55. $C_9H_8N_4OS$ requires C, 49.1; H, 3.65; N, 25.45%), $\nu_{max.}$ (KBr) 1 480 cm^{-1} (NNO), $\delta(CDCl_3)$ 4.4 (3 H, s, NMe) and 7.7 (5 H, s, Ph); 3-*benzyl*-1,2,3-*thiadiazolium*-5-*nitrosoaminide* (12c) (71%), yellow needles, had m.p. 126—128 °C (from benzene) (Found: C, 49.3; H, 3.85; N, 25.2. $C_9H_8N_4OS$ requires C, 49.1; H, 3.65; N, 25.45%), $\nu_{max.}$ (KBr) 1 490 cm^{-1} (NNO), $\delta(CDCl_3)$ 5.9 (2 H, s, $PhCH_2$), 7.5 (5 H, s, Ph), and 9.25 (1 H, s, 4-H).

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