Studies on Mesoionic Compounds. Part 7.[1] Some Aspects of the Reaction of the 1,2,3-Thiadiazolium-4-olate System

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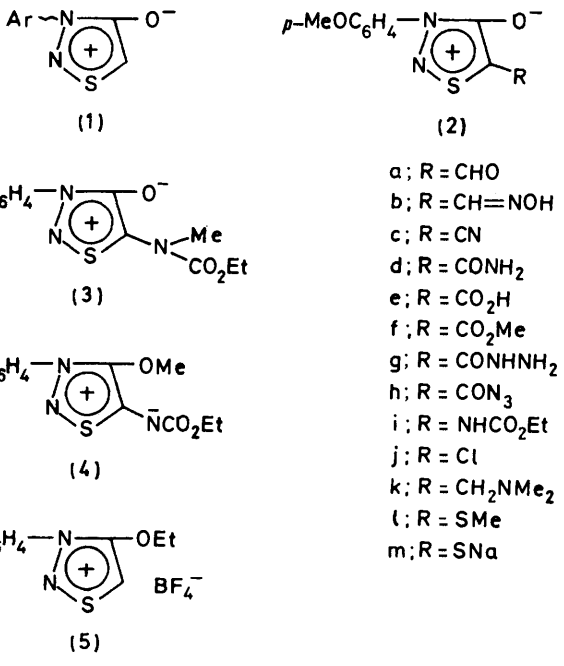
Several derivatives of mesoionic 5-substituted 1,2,3-thiadiazolium-4-olate were synthesised. The 5-amino-derivative (2i) gave a new mesoionic system, 1,2,3-thiadiazolium-5-ethoxycarbonylaminide (4), upon methylation with methyl fluorosulphonate.

SINCE the mesoionic heterocycles, 1,2,3-thiadiazolium-4-olates (1), were first synthesised by Duffin and Kendall,[2] other studies on this system have been reported.[3,4] The thiadiazole ring of the compounds (1), as well as sydnone, underwent electrophilic substitution reactions, exemplified by bromination and nitration which gave 5-bromo- and 5-nitro-derivatives, respectively.[2] Many examples of ring-opening reactions of the compounds (1) have also been described.[2,3] But their electrophilic substitution, except for the above examples and thiation,[2] have not been examined extensively. Pharmacologically, it has been found that the compounds (1) show monoamine oxidase inhibitory activity.[4]



SCHEME

During the course of our synthetic studies on mesoionic compounds, we prepared some 5-substituted derivatives of the compound (1) of pharmacological interest. Furthermore, alkylation of one of them, the 5-amino-compound (2i), gave an interesting new mesoionic 1,2,3-thiadiazolium-5-aminide derivative (4). We now detail these investigations.

RESULTS AND DISCUSSION

Direct formylation of sydnones under Vilsmeier–Haack reaction conditions have been reported.[5,6] It was found that when an *N*-phenyl group possessing an electron-releasing substituent was present in sydnone the above reaction went smoothly to afford the corresponding 4-formyl derivative in high yield.[6] Thus in our investigation 3-*p*-methoxyphenyl-1,2,3-thiadiazolium-4-olate (1; Ar = *p*-$MeOC_6H_4$) was chosen as a representative starting mesoionic compound. Treatment of the above compound with dimethylformamide–phosphorus oxychloride gave the 5-formyl derivative (2a) in 92% yield. The n.m.r. spectrum of (2a) showed a signal at δ 9.8 attributed to the formyl proton. The aldehyde function was also confirmed by the formation of the oxime (2b) on treatment with hydroxylamine. The aldoxime (2b) dehydrated under treatment with tosyl chloride–pyridine to give the nitrile (2c). However, (2c) was more favourably obtained from the formyl derivative (2a) directly *via* a Schmidt reaction (sodium azide in polyphosphoric acid). Partial hydrolysis of the nitrile (2c) with aqueous sodium hydroxide in the presence of hydrogen peroxide gave the amide (2d) in 90% yield, which was also prepared from the oxime (2b) *via* a Beckmann reaction (polyphosphoric acid at 110 °C) in a lower yield (5%). In order to obtain the 5-amino-compound the amide (2d) was then submitted to Hoffmann rearrangement under various conditions, but all attempts were unsuccessful, resulting in recovery of the amide (2d). Alkaline hydrolysis (boiling aqueous sodium hydroxide) of the nitrile (2c) and esterification of the resulting carboxylic acid (2e) with diazomethane gave the ester (2f). This carboxylic acid (2e) resembled β-keto-acids in that, on heating above its melting point, it decarboxylated to the starting mesoionic compound (1; Ar = *p*-$MeOC_6H_4$). Treatment of the ester (2f) with hydrazine hydrate in methanol at room temperature gave the hydrazide (2g) quantitatively, recrystallisation of which led to considerable decomposition. The compound (2g) was then converted to the acyl azide (2h) by treatment with sodium nitrite in hydrochloric acid at 0 °C. The i.r. spectrum of (2h) showed strong absorption bands at 2 160 and 2 100 cm^{-1}; this splitting of the azide-group stretch is well known.[7] On heating the azide (2h) in toluene in the presence of ethanol a Curtius rearrangement occurred, to yield the desired urethane derivative (2i). The i.r. spectrum of the compound (2i) showed absorptions at 3 100 (ν_{NH}), and 1 670 and 1 610 cm^{-1} (ν_{CO} of the ester and ring carbonyl, respectively). This urethane (2i) was very stable to ordinary acidic and alkaline hydrolysis.

At this point we attempted to prepare a new class of

mesoionic heterocycle, 1,2,3-thiadiazolium-5-ethoxycarbonylaminide, by alkylation of the exocyclic oxygen atom of (2i). Although Meerwein alkylation of compound (1; Ar = *p*-$MeOC_6H_4$) according to the procedure of Potts *et al.*[8] with triethyloxonium tetrafluoroborate went smoothly to yield the salt (5) in high yield, the same reaction with the urethane (2i) did not give the corresponding salt, probably due to steric factors. Thus, methylations were examined as follows. (*a*) Treatment of (2i) with diazomethane gave the corresponding *N*-methylurethane (3), m.p. 107—108 °C. The i.r. spectrum of the product (3) showed carbonyl stretching bands at 1 680 and 1 620 cm^{-1}, similar to those of (2i). The u.v. spectra of these urethanes [(2i) and (3)] were also similar. (*b*) On the other hand, methylation of (2i) with a large excess of methyl fluorosulphonate at room temperature for 48 h was incomplete, yielding the unchanged urethane (2i) (37%), the *N*-methylurethane (3) (34%), and the fluorosulphonate of the *NO*-dimethyl derivative (25%). The last salt was estimated from the n.m.r. spectrum, which showed three methyl singlets at δ 3.7, 3.85, and 3.9; it was also obtained from the reaction of the *N*-methylurethane (3) with methyl fluorosulphonate. This salt was unchanged on treatment with alkali, but it gave compound (3) on treatment with hydrochloric acid. Thus, the *O*-methyl group of this salt behaved like an enol-ether group. A similar methylation of (2i) at 60 °C was also incomplete, but the products of this reaction included the *O*-methyl derivative (4) mentioned below. Heating (2i) with methyl fluorosulphate at 95—100 °C gave the salt of the *O*-methyl derivative, the n.m.r. spectrum of which showed methyl singlets at δ 3.95 and 4.1. This salt afforded the new mesoionic compound (4), m.p. 149—151 °C, on treatment with sodium hydrogencarbonate. The i.r. spectrum of the compound (4) showed only one carbonyl stretching band at 1 580 cm^{-1}. This observation that the carbonyl absorption shifted to lower frequency compared with those of the urethanes (2i) and (3) is interpreted in terms of carbonyl polarisation, as in the case of *N*-acylsydnoneimines.[9] The mass spectra of the isomers (3) and (4) showed identical patterns, except for the fragment ion at *m/e* 295 ($M^{+\cdot} - CH_2\cdot$) in that of compound (3). In the n.m.r. spectra of compounds (3) and (4) the signals of the new methyl group were observed at δ 3.85 and 4.25, respectively. The former could be assigned to be an *N*-methyl and the latter to be an *O*-methyl group. The above methylation in the presence of a base (sodium hydrogencarbonate) at 60 °C proceeded in a short time to give the salt of the *NO*-dimethyl derivative as almost the sole product. On the basis of the above results, *O*-methylation of compound (2i) needs a high temperature, and it will probably be a kinetically controlled reaction. As expected, the new mesoionic compound (4) was unstable under acidic conditions; thus, treatment with hydrochloric acid or gaseous hydrogen chloride afforded the original urethane (2i) quantitatively. It was, however, unchanged by treatment with aqueous sodium hydroxide at 50 °C. It appears that the *N*-methylurethane (3) is thermodynamically more stable than the isomer (4); thus, when the *O*-methyl compound (4) was heated in xylene methyl migration occurred to form the *N*-methyl isomer (3).

Some electrophilic substitutions of the starting mesoionic compound (1; Ar = *p*-$MeOC_6H_4$) were also investigated. Chlorination with *N*-chlorosuccinimide, and a Mannich reaction with paraformaldehyde and dimethylamine hydrochloride, of the compound (1; Ar = *p*-$MeOC_6H_4$) proceeded smoothly to yield the 5-chloro-derivative (2j) and 5-dimethylaminomethyl derivative (2k) in high yield, respectively. One of us (K. M.) has reported previously on the synthesis of 4-thiosydnones[10] of pharmacological interest. Application of this procedure to the present mesoionic system (1) was exemplified by the introduction of a methylthio-group. Treatment of compound (1; Ar = *p*-$MeOC_6H_4$) with dimethyl sulphoxide and acetyl chloride yielded the 5-methylthio-derivative (2l) in 82% yield. This product was also prepared by the action of methyl iodide on the 5-sodiothio-derivative (2m), obtained by heating the original mesoionic compound (1; Ar = *p*-$MeOC_6H_4$) with sodium sulphide in aqueous ethanol.[2] Pharmacological tests of the above compounds are under progress, and will be presented elsewhere.

EXPERIMENTAL

M.p.s were determined with a Yanagimoto hot-stage apparatus. I.r. spectra were measured with a JASCO IRA-1 spectrophotometer, and u.v. spectra were measured for solutions in ethanol with a Hitachi 124 spectrophotometer. N.m.r. spectra were obtained on a JEOL JNM-PMX-60 spectrometer with tetramethylsilane as internal standard. Mass spectra were obtained with a JEOL JMS-01SG-2 instrument.

5-Formyl-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (2a).—To a cooled mixture of dimethylformamide (6.3 g) and phosphorus oxychloride (13 g) was added a solution of 3-*p*-methoxyphenyl-1,2,3-thiadiazolium-4-olate[2] (6 g) in chloroform (50 ml), and the mixture was refluxed for 2 h. The chloroform was evaporated off, and the residue diluted with ice–water. The precipitate was collected and recrystallised from ethyl acetate to give the *formyl derivative* (2a) (6.3 g, 92%) as yellow needles, m.p. 147—149 °C (Found: C, 50.65; H, 3.35; N, 11.90. $C_{10}H_8N_2O_3S$ requires C, 50.84; H, 3.41; N, 11.86%); $\nu_{max.}$ (KBr) 1 630 cm^{-1} (CO); $\lambda_{max.}$ 232 (log ε 4.25), 305 (3.71), and 405 nm (3.95); δ($CDCl_3$) 3.9 (3 H, s, OMe), 7.0 and 7.9 (4 H, AB q, *J* 9 Hz, aromatic), and 9.7 (1 H, s, CHO).

5-Hydroxyiminomethyl-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (2b).—A mixture of the formyl derivative (2a) (2.35 g) and hydroxylamine hydrochloride (1.01 g) in ethanol (30 ml) and pyridine (30 ml) was stirred at room temperature for 2 h. Concentration, and then dilution with water, gave a crystalline product, which was collected and dried to yield the *oxime* (2b) (2.29 g, 91%). Recrystallisation from methanol–benzene afforded yellow plates, m.p. 179—182 °C (Found: C, 47.6; H, 3.5; N, 16.65. $C_{10}H_9N_3O_3S$ requires C, 47.80; H, 3.61; N, 16.73%); $\nu_{max.}$ (KBr) 3 000—2 600 (OH), 1 600 (C=N), and 1 570 cm^{-1} (CO); $\lambda_{max.}$ 234 (log ε 3.70), 318 (2.78), and 413 nm (3.48).

5-Cyano-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (2c).—(*a*) The formyl derivative (2a) (5.4 g) was dissolved in polyphosphoric acid [prepared from 85% phosphoric acid (50 g) and phosphorus pentaoxide (25 g)] and cooled to 0 °C. To this solution was added portionwise sodium azide (2.6 g) at 0—5 °C, and the mixture was stirred at this temperature for 3 h. After dilution with water, the precipitate was collected and recrystallised from methanol to give the *nitrile* (2c) (4.5 g, 84%) as yellow needles, m.p. 177—178 °C (Found: C, 51.75; H, 3.0; N, 17.85. $C_{10}H_7N_3O_2S$ requires C, 51.49; H, 3.03; N, 18.02%); $\nu_{max.}$ (KBr) 2 210 (CN) and 1 660 cm^{-1} (CO); $\lambda_{max.}$ 223 (log ε 4.25), 325 (3.60), and 412 nm (4.15); *m/e* 233 (M^+).

(*b*) A mixture of the oxime (2b) (1.63 g) and toluene-*p*-sulphonyl chloride (1.5 g) in pyridine (20 ml) was heated on an oil-bath at 50 °C for 16 h. The mixture was poured onto ice–water, and the precipitate collected and recrystallised from methanol to give the *nitrile* (2c) (0.8 g, 53%), m.p. 176—178 °C. This product was identical with the product obtained by procedure (*a*) on the basis of i.r. spectra and mixed melting-point measurement.

5-Carbamoyl-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (2d).—(*a*) A mixture of the nitrile (2c) (1 g), 20% sodium hydroxide (1 ml), and 30% hydrogen peroxide (2 ml) in methanol (20 ml) was refluxed for 2.5 h. After concentration, the residual crystalline material was washed with water and recrystallised from ethanol to give the *amide* (2d) (778 mg, 90%) as yellow needles, m.p. 188—191 °C (Found: C, 48.0; H, 3.3; N, 16.55. $C_{10}H_9N_3O_3S$ requires C, 47.80; H, 3.61; N, 16.73%); $\nu_{max.}$ (KBr) 3 380, 3 250 (NH_2), and 1 630 and 1 580 cm^{-1} (CO); $\lambda_{max.}$ 225 (log ε 4.0), 320 (3.0), and 405 nm (3.78); δ([$^2H_6$]DMSO) 3.9 (3 H, s, OMe), 7.0 and 7.85 (4 H, AB q, *J* 9 Hz, aromatic), and 7.4—8.0 (2 H, br s, NH_2).

(*b*) A suspension of the oxime (2b) (76 mg) in polyphosphoric acid [prepared from phosphorus pentaoxide (3 g) and 85% phosphoric acid (6 g)] was heated at 110 °C for 3 h. The mixture was poured onto ice, and neutralised with potassium carbonate. The precipitate was collected and recrystallised from methanol–isopropyl alcohol to give the *amide* (2d) (4 mg, 5%) as yellow leaflets, m.p. 190—192 °C. This product was identical with the amide obtained in the (*a*) by comparison of i.r. spectra.

5-Carboxy-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (2e).—A mixture of the nitrile (2c) (186 mg) and 10% sodium hydroxide (4.5 ml) was refluxed for 2 h. After cooling, the mixture was made acidic with concentrated hydrochloric acid. Extraction with chloroform and evaporation gave the *carboxylic acid* (2e) (158 mg, 79%), m.p. 138—140 °C. Recrystallisation from n-hexane–benzene gave an analytical sample, yellow needles, m.p. 140—141 °C (Found: C, 47.45; H, 3.35; N, 11.05. $C_{10}H_8N_2O_4S$ requires C, 47.61; H, 3.19; N, 11.10%); $\nu_{max.}$ (KBr) 3 000—2 500, 1 710 (CO_2H), and 1 610 cm^{-1} (CO); δ($CDCl_3$) 3.9 (3 H, s, OMe), 7.05 and 8.0 (4 H, AB q, *J* 9 Hz, aromatic), and 8.5 (1 H, br s, CO_2H).

Decarboxylation of Compound (2e).—The carboxylic acid (2e) (50 mg) was heated at 150 °C. After the evolution of carbon dioxide had ceased (30 min), the molten material was crystallised from ethanol to give 3-p-*methoxyphenyl-1,2,3-thiadiazolium-4-olate* (25 mg, 61%) as yellow leaflets, m.p. 143—145 °C. This product was identical with an authentic sample by comparison of i.r. spectra.

5-Methoxycarbonyl-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (2f).—To a solution of the carboxylic acid (2e) (2.9 g) in chloroform (100 ml) was added a solution of diazomethane in ether [prepared from *N*-nitroso-*N*-methylurea (20 g), 50% potassium hydroxide (60 ml), and ether (150 ml)] at room temperature. After 30 min, evaporation and recrystallisation of the residue from methanol gave the *methyl ester* (2f) (2.42 g, 79%) as yellow needles, m.p. 169—172 °C (Found: C, 49.45; H, 3.6; N, 10.5. $C_{11}H_{10}N_2O_4S$ requires C, 49.62; H, 3.79; N, 10.52%); $\nu_{max.}$ (KBr) 1 720 and 1 660 cm^{-1} (CO); δ($CDCl_3$) 3.9 (3 H, s, OMe), 3.95 (3 H, s, OMe), and 6.95 and 7.9 (4 H, AB q, *J* 9 Hz, aromatic); *m/e* 266 (M^+).

5-Hydrazinocarbonyl-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (2g).—The ester (2f) (688 mg) was dissolved in chloroform (5 ml) and mixed with 85% hydrazine hydrate (1.13 g) and methanol (40 ml). The mixture was stirred at room temperature for 4.5 h. Dilution with chloroform (100 ml), washing with water, and evaporation gave the *hydrazide* (2g) (658 mg, 96%) as yellow crystals, m.p. 168—170 °C. This product was of satisfactory purity (recrystallisation caused considerable decomposition) (Found: C, 44.9; H, 3.75; N, 21.05. $C_{10}H_{10}N_4O_3S$ requires C, 45.10; H, 3.79; N, 21.04%); $\nu_{max.}$ (KBr) 3 300 (NH_2), and 1 670 and 1 620 cm^{-1} (CO); δ($CDCl_3$) 3.85 (3 H, s, OMe), 4.0 (2 H, s, NH_2), 6.9 and 7.8 (4 H, AB q, *J* 9 Hz, aromatic), and 9.0 (1 H, br s, CONH).

5-Ethoxycarbonylamino-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (2i).—To a cooled suspension of the hydrazide (2g) (460 mg) in 10% hydrochloric acid (20 ml) was added dropwise a solution of sodium nitrite (140 mg) in water (5 ml) at 0 °C with stirring. After stirring for an additional 1.5 h, the yellow precipitate was collected, washed with water, and dried to afford *5-azidocarbonyl-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate* (2h) (466 mg, 97%), m.p. 225—230 °C (decomp.); $\nu_{max.}$ (KBr) 2 160, 2 100 (N_3), and 1 670 and 1 640 cm^{-1} (CO).

The above azide (2h) (279 mg) was added to dry toluene (15 ml) and absolute ethanol (4 ml), and refluxed for 2 h. Concentration and recrystallisation of the residue from ethanol gave the *urethane* (2i) (173 mg, 59%) as yellow leaflets, m.p. 215—218 °C (Found: C, 48.8; H, 4.25; N, 14.7. $C_{12}H_{13}N_3O_4S$ requires C, 48.80; H, 4.44; N, 14.23%); $\nu_{max.}$ (KBr) 3 100 (NH), and 1 670 and 1 610 cm^{-1} (CO); $\lambda_{max.}$ 226 (log ε 4.13), 315 (3.79), and 386 nm (3.94); δ($CDCl_3$) 1.25 (3 H, t, *J* 7 Hz, Me), 3.85 (3 H, s, OMe), 4.3 (2 H, q, *J* 7 Hz, CH_2), and 7.25 and 8.4 (4 H, AB q, *J* 9 Hz, aromatic); *m/e* 295 (M^+).

5-N-Ethoxycarbonylmethylamino-3-p-methoxyphenyl-1,2,3-thiadiazolium-4-olate (3).—(*a*) To a solution of the urethane (2i) (100 mg) in chloroform (15 ml) was added a solution of diazomethane in ether [prepared from *N*-nitroso-*N*-methylurea (1 g), 50% potassium hydroxide (5 ml), and ether (10 ml)], and the mixture was allowed to stand at room temperature for 30 min. Concentration and recrystallisation of the residue from isopropyl ether gave the *N-methylurethane* (3) (63 mg, 60%) as yellow needles, m.p. 107—108 °C (Found: C, 50.5; H, 4.85; N, 13.5. $C_{13}H_{15}N_3O_4S$ requires C, 50.46; H, 4.89; N, 13.58%); $\nu_{max.}$ (KBr) 1 670 and 1 620 cm^{-1} (CO); $\lambda_{max.}$ 322 (log ε 3.38) and 400 nm (4.02); δ($CDCl_3$) 1.35 (3 H, t, *J* 7 Hz, Me), 3.85 (6 H, s, OMe and NMe), 4.35 (2 H, q, *J* 7 Hz, CH_2), and 6.9 and 7.9 (4 H, AB q, *J* 9 Hz, aromatic); *m/e* 309 (M^+).

(*b*) A mixture of the urethane (2i) (295 mg), sodium hydrogencarbonate (1 g), and methyl fluorosulphonate (1 g) in chloroform (5 ml) was heated on an oil-bath at 60 °C for 15 min. After dilution with chloroform (10 ml), the mixture

was washed with water and dried. Evaporation of the chloroform gave a yellow viscous oil (420 mg); δ($CDCl_3$) 1.4 (3 H, t, *J* 7 Hz, Me), 3.7 (3 H, s, NMe), 3.85 (3 H, s, OMe), 3.9 (3 H, s, OMe), 4.45 (2 H, q, *J* 7 Hz, CH_2), and 7.0 and 7.7 (4 H, AB q, *J* 9 Hz, aromatic). This oil was dissolved in concentrated hydrochloric acid (2 ml) and stirred at room temperature for 10 min. Neutralisation with sodium hydrogencarbonate, extraction with chloroform, and the usual work-up of the extract gave the N-*methylurethane* (3) (269 mg, 87%) as yellow needles, m.p. 106—108 °C (from isopropyl ether). The i.r. spectrum of this product was identical with that of the compound obtained in (*a*).

4-*Methoxy*-3-p-*methoxyphenyl*-1,2,3-*thiadiazolium*-5-*ethoxycarbonylaminide* (4).—A mixture of the compound (2i) (295 mg) and methyl fluorosulphonate (1 g) was heated on an oil-bath at 95—100 °C for 3 h. After concentration of the mixture, the residue was washed with ether, and then triturated with isopropyl alcohol–ether with cooling to precipitate the salt. The precipitate was collected and washed with ether to give a pale yellow crystalline mass (294 mg); δ[$(CD_3)_2CO$] 1.25 (3 H, t, *J* 7 Hz, Me), 3.95 (3 H, s, OMe), 4.1 (3 H, s, OMe), 4.45 (2 H, q, *J* 7 Hz, CH_2), and 7.25 and 7.85 (4 H, AB q, *J* 9 Hz, aromatic). To a suspension of the above crystals in chloroform was added a saturated aqueous solution of sodium hydrogencarbonate and stirred for 10 min. The chloroform layer was worked-up as usual to yield the 5-*ethoxycarbonylaminide* (4) (185 mg, 60%) as orange-yellow needles, m.p. 149—151 °C (Found: C, 50.2; H, 4.95; N, 13.7. $C_{13}H_{15}N_3O_4S$ requires C, 50.46; H, 4.89; N, 13.58%); $\nu_{max.}$ (KBr) 1 580 cm^{-1} (CO); $\lambda_{max.}$ 221 (log ε 4.19), 242 (4.08), 292 (3.84), and 365 nm (3.99); δ($CDCl_3$) 1.35 (3 H, t, *J* 7 Hz, Me), 3.9 (3 H, s, OMe), 4.25 (3 H, s, OMe), 4.3 (2 H, q, *J* 7 Hz, CH_2), and 6.9 and 7.45 (4 H, AB q, *J* 9 Hz, aromatic); *m/e* 309 (M^+).

Other Examples of Methylation of the Urethane (2i).—(*a*) A mixture of the compound (2i) (295 mg) and methyl fluorosulphonate (1 g) in chloroform (10 ml) was stirred at room temperature for 48 h. The mixture was washed with water, 10% potassium carbonate, and water. The chloroform solution was dried and evaporated. The residue was dissolved in hot isopropyl alcohol and cooled to crystallise the *urethane* (2i) (110 mg, 37% recovery). The mother-liquor was concentrated, and the residue was chromatographed on alumina (Merck, basic, 2 g). Elution with benzene gave the N-*methylurethane* (3) (106 mg, 34%), m.p. 103—107 °C (from isopropyl ether). Further elution with chloroform gave a *yellow oil* (106 mg), i.r. and n.m.r. spectra of which were identical with that of the oily product obtained in the above procedure for preparation of the *N*-methylurethane (3).

(*b*) A mixture of the compound (2i) (295 mg) and methyl fluorosulphonate (1 g) was heated on an oil-bath at 60 °C for 3 h. After concentration of the mixture, the residue was dissolved in chloroform and washed with saturated aqueous solution of sodium hydrogencarbonate and water. The usual work-up of the chloroform solution gave a residue, consisting of oil and crystals. Recrystallisation of the residue from isopropyl alcohol afforded the unchanged urethane (2i) (49 mg, 16.6% recovery). The mother-liquor was evaporated, and the residue was triturated with hot isopropyl ether. On cooling the isopropyl ether solution gave the O-*methyl derivative* (4) (45 mg, 14.5%) as yellow needles, m.p. 139—145 °C. Further concentration of the solution gave the N-*methylurethane* (3) (43 mg, 14%) as fine yellow needles, m.p. 100—105 °C. These products were identical with the corresponding authentic samples by comparison of i.r. and n.m.r. spectra.

4-*Ethoxy*-3-p-*methoxyphenyl*-1,2,3-*thiadiazolium Tetrafluoroborate* (5).—To a suspension of the compound (1; Ar = *p*-$MeOC_6H_4$) (2 g) in dichloromethane (15 ml) was added a solution of triethyloxonium tetrafluoroborate [11] (3.57 g) in dichloromethane (5 ml) at room temperature and the mixture was stirred overnight. Evaporation and recrystallisation of the residue from isopropyl alcohol gave the *salt* (5) (2.7 g, 89%) as pale yellow sticks, m.p. 129—130 °C (Found: C, 41.0; H, 4.25; N, 8.75. $C_{11}H_{13}BF_4N_2O_2S$ requires C, 40.76; H, 4.04; N, 8.64%); δ[$(CD_3)_2CO$] 1.5 (3 H, t, *J* 7 Hz, Me), 3.95 (3 H, s, OMe), 4.7 (2 H, q, *J* 7 Hz, CH_2), 7.2 and 7.8 (4 H, AB q, *J* 9 Hz, aromatic), and 9.2 (1 H, s, 5-H).

5-*Chloro*-3-p-*methoxyphenyl*-1,2,3-*thiadiazolium*-4-*olate* (2j).—A mixture of compound (1; Ar = *p*-$MeOC_6H_4$) (2 g) and *N*-chlorosuccinimide (1.5 g) in chloroform (50 ml) was refluxed for 5 h. After cooling the mixture was washed with water and evaporated. The residue was then chromatographed on silica gel (Merck, 70—230 mesh, 5 g). Elution with benzene gave crystalline material, which was recrystallised from isopropyl alcohol to give the 5-*chloro-derivative* (2j) (1.88 g, 81%) as yellow cubes, m.p. 126—128 °C (Found: C, 44.30; H, 2.65; N, 11.75. $C_9H_7ClN_2O_2S$ requires C, 44.54; H, 2.91; N, 11.73%); $\nu_{max.}$ (KBr) 1 620 cm^{-1} (CO); $\lambda_{max.}$ 226 (log ε 4.25), 313 (3.88), and 397 nm (4.18); δ(CCl_4) 3.8 (3 H, s, OMe), and 6.8 and 7.6 (4 H, AB q, *J* 9.Hz, aromatic).

5-NN-*Dimethylaminomethyl*-3-p-*methoxyphenyl*-1,2,3-*thiadiazolium*-4-*olate* (2k).—A mixture of compound (1; Ar = *p*-$MeOC_6H_4$) (1.01 g), paraformaldehyde (160 mg), and dimethylamine hydrochloride (430 mg) in acetic acid (5 ml) was heated on an oil-bath at 80 °C for 5 h. The mixture was diluted with water (10 ml) and neutralised with potassium carbonate. Extraction with chloroform and the usual work-up of the extract gave the 5-*dimethylaminomethyl derivative* (2k) (1.04 g, 81%) as yellow needles, m.p. 88—92 °C (from isopropyl ether) (Found: C, 54.05; H, 6.0; N, 15.8. $C_{12}H_{15}N_3O_2S$ requires C, 54.32; H, 5.70; N, 15.84%); $\nu_{max.}$ (KBr) 1 630 cm^{-1} (CO); $\lambda_{max.}$ 220 (log ε 4.20), 302 (3.76), and 385 nm (4.08); δ($CDCl_3$) 2.4 (6 H, s, NMe_2), 3.7 (2 H, s, CH_2), 3.9 (3 H, s, OMe), and 6.9 and 7.9 (4 H, AB q, *J* 9 Hz, aromatic); *m/e* 265 (M^+).

3-p-*Methoxyphenyl*-5-*methylthio*-1,2,3-*thiadiazolium*-4-*olate* (2l).—(*a*) To a stirred suspension of compound (1; Ar = *p*-$MeOC_6H_4$) (800 mg) in dimethyl sulphoxide (1.2 g) was added acetyl chloride (600 mg), and the mixture was stirred at room temperature overnight. After dilution with water, the mixture was extracted with chloroform. The extract was washed with aqueous solution of sodium hydrogencarbonate, and worked up as usual to give the 5-*methylthio-derivative* (2l) (805 mg, 82%) as yellow leaflets, m.p. 101—103 °C (from n-hexane–ethyl acetate) (Found: C, 47.45; H, 4.0; N, 11.25. $C_{10}H_{10}N_2O_2S_2$ requires C, 47.22; H, 3.96; N, 11.02%); $\nu_{max.}$ (KBr) 1 610 cm^{-1} (CO); δ($CDCl_3$) 2.55 (3 H, s, SMe), 3.9 (3 H, s, OMe), and 7.0 and 8.0 (4 H, AB q, *J* 9 Hz, aromatic); *m/e* 254 (M^+).

(*b*) To a solution of compound (1; Ar = *p*-$MeOC_6H_4$) (6 g) in ethanol (60 ml) was added sulphur (1.1 g) and a solution of sodium sulphide nonahydrate (7.5 g) in 95% ethanol (30 ml), and the mixture was refluxed for 1.5 h. After concentration water (30 ml) was added to the residue and the solution was filtered. To the filtrate was added a

saturated aqueous solution of sodium chloride, which caused a yellow crystalline mass to separate. The precipitate was collected and recrystallised from isopropyl alcohol to give the *5-sodiothio-derivative* (2m) (2.9 g, 38.5%) as yellow needles, m.p. 150—156 °C (Found: C, 40.95; H, 2.85; N, 10.4. $C_9H_7N_2NaO_2S_2$ requires C, 41.21; H, 2.69; N, 10.68%); $\nu_{max.}$ (KBr) 1 550 cm^{-1} (CO).

A mixture of the above compound (2m) (200 mg), methyl odide (600 mg), and potassium carbonate (111 mg) in methanol (10 ml) was refluxed for 9 h. After concentration, the residue was diluted with benzene and filtered. The filtrate was washed with brine and evaporated. Recrystallisation of the residue from a small amount of benzene gave the *5-methylthio-derivative* (2l) (173 mg, 93%) as yellow leaflets, m.p. 101—103 °C. This product was identified with the product obtained in procedure (*a*) on the basis of i.r. spectra and mixed melting-point measurement.

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