*Giuseppe Werber, Francesco Buccheri and Manlio Gentile*

Istituto di Chimica Organica- Facoltà di Scienze dell'Università, Via Archirafi 20, Palermo, Italy

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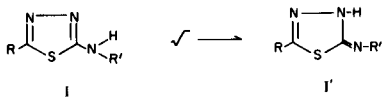
The synthesis of some 2-amino-5-bromo-1,3,4-thiadiazoles is reported; these substrates are found to behave as ambident nucleophiles in alkylation, acylation and nitrosation reactions, giving thiadiazoliens along with thiadiazole derivatives. This finding suggests amine-imine tautomerism between these compounds and the corresponding $\Delta^2$-1,3,4-thiadiazolines.

*J. Heterocyclic Chem.*, 14, 823 (1977)

**PROPER SAFEGUARDS SHOULD BE TAKEN TO PREVENT EXPOSURE TO THE THIADIAZOLINES 3f, 4f AND 4a·HI BOTH DURING AND AFTER THEIR PREPARATION. IT IS RECOMMENDED THAT ALL OPERATION INVOLVING THESE COMPOUNDS BE CARRIED OUT IN A GOOD HOOD. THESE COMPOUNDS ARE SKIN IRRITANTS AND REPEATED EXPOSURE TO EVEN VERY VERY LOW CONCENTRATIONS CAUSES INCREASED SENSITIVITY TO THE SUBSTANCES (ALLERGY).**

Our previous studies on 2-amino-5-benzoyl-1,3,4-thiadiazoles (1) have shown that these compounds behave as ambident nucleophiles in methylation reactions. This might be interpreted on basis of amine-imine tautomerism, which is a well established phenomenon for cyclic thiamidines (Equation I).



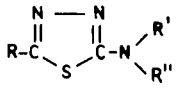
I I'

In continuation of our research in the field, we decided to synthesize a number of 2-amino-1,3,4-thiadiazoles substituted with bromine at the 5-position, with the aim of verifying whether, similarly to 5-benzoyl derivatives in alkylation, these substrates also behave as ambident nucleophiles not only on alkyaltion but also on acylation and nitrosation. The study was planned to investigate also the behaviour of 2-nitroso and 2-*N*-acyl derivatives for which a prototropic equilibrium such as in Equation I can also be envisaged.

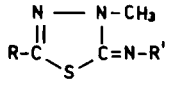
Compounds **2b-i** and **4a-f** were previously unreported in the literature and are described in this study for the first time. In order to obtain model disubstituted compounds, which are necessary for structural assignment of the thiadiazolines produced, the hydroiodide of $\Delta^2$-1,3,4-thiadiazoline, **4a** was also employed in alkylation, nitrosation and acylation reactions (Scheme I).

In a previous study (2) we have reported the synthesis of compounds **1a-i** and **3a-f**. Compounds **1a-i**, by reacting with bromine in acetic acid (either in the presence or absence of sodium acetate), yielded brominated aminothiadiazoles **2a-i**. On the other hand, thiadiazolidine **3a**,

SCHEME I



1 a-i R=H
2 a-i R=Br



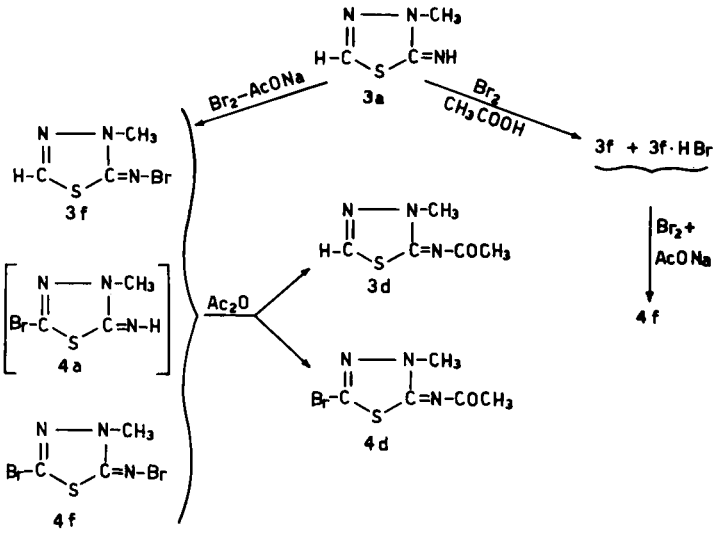
3 a-f R=H
4 a-f R=Br

a : R'=R''=H
b : R'=H ; R''=$CH_3$
c : R'=H ; R''=NO
d : R'=H ; R''=$COCH_3$
e : R'=H ; R''=$COC_6H_5$
f : R'=R''=$CH_3$
g : R'=$CH_3$ ; R''=NO
h : R'=$CH_3$ ; R''=$COCH_3$
i : R'=$CH_3$ ; R''=$COC_6H_5$

a : R'=H
b : R'=$CH_3$
c : R'=NO
d : R'=$COCH_3$
e : R'=$COC_6H_5$
f : R'=Br

by reacting with bromine-acetic acid in the presence of sodium acetate yielded a mixture that tlc analysis show to be composed by 2-bromo-4-methyl-5-bromoimino-$\Delta^2$-1,3,4-thiadiazoline (**4f**), 4-methyl-5-bromoimino-$\Delta^2$-1,3,4-thiadiazoline (**3f**), plus a third compound which resisted attempts at isolation because of its instability (Scheme

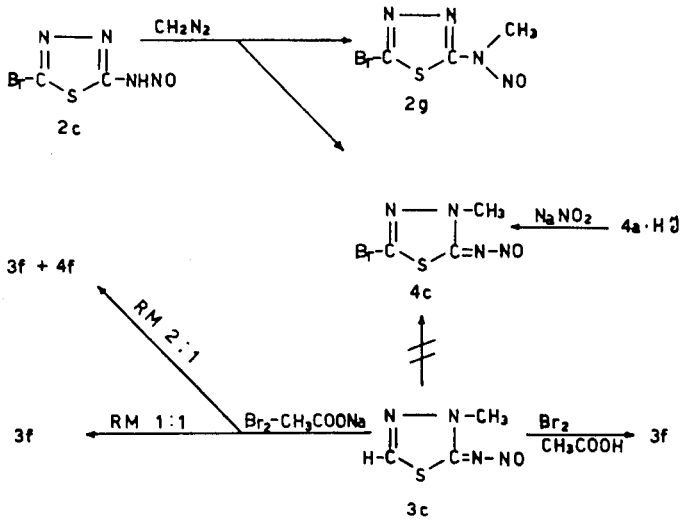
SCHEME II



II). To this we attribute the structure of 2-bromo-4-methyl-5-imino-$\Delta^2$-1,3,4-thiadiazoline (**4a**) on the basis of the following evidence. The aforementioned mixture of **4f**, **3f** and the unknown, when treated with acetic anhydride, yielded acetyl derivatives **3d** and **4d** as the sole products. Clearly, **3d** was produced by **3f**, but **4f** and the unknown can both yield the same acetyl derivative **4d** only if the unknown has structure **4a**. Consistent with this, we found that the hydroiodide salt of **4a** produces the acetyl derivative **4d** on reaction with acetic anhydride. The same **4d** was produced on acetylation of **4f**, whereas **3f** yielded **3d**. Furthermore, treatment of the mixture of the three compounds above with carbon tetrachloride removed **3f**, whereas **4f** and the unknown were not appreciably soluble in this solvent. Upon dissolving the residue in deuteriochloroform and determining the $^1$H-nmr spectrum, one singlet at $\delta$ 3.54 was exhibited in the region of N-C$H_3$ resonances, and one broad signal at *ca.* $\delta$ 11.5, characteristic of N-H resonance. The two resonance peaks integrate 6:1. As it is likely that N-$CH_3$ signals for **4a** and **4f** overlap at $\delta$ 3.54, the integration ratio above seems to indicate that **4f** and **4a** are produced in the ratio of *ca.* 1:1 in the bromination of **3a** in acetic acid in the presence of sodium acetate. In the absence of sodium acetate, instead, just **3f**, along with the corresponding hydrobromide, was produced in the same reaction. In the presence of sodium acetate, with an excess of bromine, **3a** produced just the dibromothiadiazoline **4f**, as expected.

The reaction of the *N*-nitroso derivative **3c** with stoicheiometric bromine in acetic acid did not yield the 5-substituted bromine derivative **4c**, as might have been expected, but it gave the thiadiazoline **3f**. Carrying out the reaction in the presence of sodium acetate did not change this result. Excess bromine, instead, again produced the dibromoderivative **4f** along with **3f**. (Scheme III).

SCHEME III




Bromination of thiadiazolines **3b** and **3d-f** smoothly gave the corresponding 5-bromo derivatives **4b** and **4d-f**, respectively.

Treatment of aminothiadiazole **2a** with methyl iodide produced the hydroiodide of the imino compound **4a**. Although, as mentioned previously, **4a** was quite unstable (see Experimental), it can be fully characterized *via* its derivatives. Nitrosation, acetylation and benzoylation reactions can be carried out on **2a**, yielding the expected thiadiazoles **2c**, **2d**, and **2e**, respectively.

Treatment of **2b** with nitrous acid yielded **2g**, whereas reaction with methyl iodide gave 2-bromo-4-methyl-5-methylimino-$\Delta^2$-1,3,4-thiadiazoline hydroiodide, from this the corresponding base **4b** could be freed by treatment with bases. Acylation of **2b** was easily performed, obtaining acetyl derivative **2h** and benzoyl derivative **2i**.

Starting with the nitroso derivative **2c**, treatment with acetic anhydride afforded removal of the NO group, yielding the acetyl derivative **2d**. Attempted benzoylation of the same **2c** using benzoyl chloride, instead, resulted in extensive decomposition. Treatment of **2c** with nitrous acid led to recovery of unchanged starting material; reaction of the same compound with diazomethane gave a mixture of thiadiazole **2g** and thiadiazoline **4c** in low yields.

By way of contrast, alkylation of substrate **2d** produced a mixture of **2h** and **4d** in good yields. However, attempts to perform nitrosation or acetylation of **2d** failed, the starting material being recovered unchanged. Attempted benzoylation resulted in extensive substrate decomposition.

Reaction of thiadiazole **2e** with acetic anhydride yielded replacement of the benzoyl group by acetyl, giving **2d**. Alkylation of **2e** again produced a mixture of **2i** and **4e**, whereas it was unreactive toward nitrous acid, and substrate decomposition was observed in attempting benzoylation with benzoyl chloride.

The hydroiodide of thiadiazoline **4a** readily undergoes alkylation, nitrosation, acetylation and benzoylation, yielding thiadiazolines **4b**, **4c**, **4d** and **4e**, respectively.

In conclusion, all of the substrates examined, but for thiadiazoline **3c**, were found to react with bromine in acetic acid, yielding substitution by bromine at the heterocyclic C-H and/or bromination at the exocyclic nitrogen. The 5-bromothiadiazoles are found to behave as ambident nucleophiles in alkylation, nitrosation and acylation reactions; this fact supports the hypothesis that prototropic tautomeric equilibria might be established among the 2-amino-1,3,4-thiadiazole and the corresponding 5-imino-$\Delta^2$-1,3,4-thiadiazoline form for this class of heterocyclic compounds.

For the compounds reported in this study, the structure assigned agreed with the ir and the $^1$H-nmr spectral data and with elemental analyses.

## EXPERIMENTAL

Melting points were determined using a Kofler hotplate and are uncorrected. Ir spectra (nujol mull) were recorded on a Perkin-Elmer Infracord 137 instrument. Nmr spectra (60 MHz) were obtained using a Jeol C-60 H spectrometer with TMS as the internal standard. The structure of all products described was established by elemental analysis and by their spectroscopic data, as well as by comparison (ir spectra, melting points, mixed melting points) with authentic samples when available. Elemental analyses data are given only for new compounds, previously unreported.

Bromination of **1a-i** and of **3a-f**. General Procedure.

To 0.01227 mole of the heterocyclic compound, dissolved or suspended in 17.5 ml. of acetic acid, 4 g. of dry sodium acetate was added; then 6.5 ml. of 2*M* solution of bromine in acetic acid was added dropwise, while the reaction mixture was being stirred (for **1d-e,h-i** and **3d-e**, 10 ml. of the said bromine in acetic acid solution was added, and then mixture refluxed; for **3e** better results were obtained if sodium acetate was absent). Stirring was maintained until the reaction solution colour turned deep orange. The solvent was partially removed *in vacuo* and upon dilution of the residue with water, the crude product precipitates out, or it can be extracted in a suitable organic solvent.

Following the above procedure the following compounds were obtained.

2-Amino-5-bromo-1,3,4-thiadiazole (**2a**) (3).

This compound was obtained from **1a** (1.24 g.) in 87% yield (1.92 g.), m.p. 182-183° (ethanol); ir: 3311, 3077 $cm^{-1}$ ($NH_2$); nmr (DMSO-$d_6$): 7.47 δ (s, 2H, $NH_2$).

*Anal.* Calcd. for $C_2H_2BrN_3S$: C, 13.34; H, 1.12; N, 23.34. Found: C, 13.30; H, 1.10; N, 23.65.

2-Methylamino-5-bromo-1,3,4-thiadiazole (**2b**).

From **1b** (1.4 g.) after extraction with chloroform of the diluted reaction mixture, 1.9 g., yield 80% of **2b**, m.p. 123-124° (benzene-ligroin), was obtained; ir: 3155 $cm^{-1}$ (NH); nmr (DMSO-$d_6$): 2.86 δ (d, 3H, NH-$CH_3$, J = 4.9 Hz), 7.86 δ (br. s, 1H, $NHCH_3$).

*Anal.* Calcd. for $C_3H_4BrN_3S$: C, 18.57; H, 2.07; N, 21.65. Found: C, 18.40; H, 1.95; N, 21.60.

Sodium Salt of 2-Nitrosoamino-5-bromo-1,3,4-thiadiazole (**2c**).

Compound **1c** (1.6 g.) gave 2.4 g., yield 85%, of **2c** after crystallization from water, m.p. > 330°.

*Anal.* Calcd. for $C_2N_4BrOSNa \cdot H_2O$: C, 9.64; H, 0.81; N, 22.50. Found: C, 10.01; H, 0.80; N, 22.28.

This sodium salt of **2c** in 15% aqueous hydrochloric acid gave **2c**, m.p. > 310° (DMSO).

*Anal.* Calcd. for $C_2HBrN_4OS$: C, 11.48; H, 0.48; N, 26.80. Found: C, 11.80; H, 0.51; N, 26.57.

The sodium salt of **2c** can be prepared by treating **2c** (1 g.) with 1% aqueous sodium hydroxide with gentle heating until solution was complete. The sodium salt slowly separates out.

2-Acetylamino-5-bromo-1,3,4-thiadiazole (**2d**).

Compound **1d** (1.75 g.) gave **2d** (1.8 g., 66%), m.p. 243-244° (ethanol); ir: 3058 (NH) and 1667 $cm^{-1}$ (C=O); nmr (DMSO-$d_6$): 2.22 δ (s, 3H, $COCH_3$), 11-13 δ (br. s, 1H, NH).

*Anal.* Calcd. for $C_4H_4BrN_3OS$: C, 21.63; H, 1.81; N, 18.92. Found: C, 21.50; H, 1.70; N, 19.05.

2-Benzoylamino-5-bromo-1,3,4-thiadiazole (**2e**).

Compound **1e** (2.5 g.) gave **2e** (2.8 g., 80%), m.p. 246-247° (ethanol); ir: 3077 (NH) and 1664 $cm^{-1}$ (C=O); nmr (DMSO-$d_6$): 7.51-8.78 δ (m, 5H, Ar-H), 8.49 δ (br. s, 1H, NH).

*Anal.* Calcd. for $C_9H_6BrN_3OS$: C, 38.04; H, 2.13; N, 14.79. Found: C, 37.85; H, 2.08; N, 15.00.

2-Dimethylamino-5-bromo-1,3,4-thiadiazole (**2f**).

Compound **1f** (1.6 g.) gave **2f** (2.47 g., 97%) after extraction of the crude reaction product in chloroform, m.p. 85-86° (ligroin); nmr (DMSO-$d_6$): 3.04 δ (s, 6H, $N(CH_3)_2$).

*Anal.* Calcd. for $C_4H_6BrN_3S$: C, 23.09; H, 2.90; N, 20.19. Found: C, 22.90; H, 2.95; N, 20.25.

2-Methylnitrosoamino-5-bromo-1,3,4-thiadiazole (**2g**).

Compound **1g** (1.77 g.) gave, after extraction of the diluted reaction mixture with chloroform, a mixture (2.05 g.) of starting material and of the brominated product; dry column chromatography (silica gel GF 254, cyclohexane-ethylacetate 2:1) affords 0.5 g. of unreacted **1g** and 2-methylnitrosoamino-5-bromo-1,3,4-thiadiazole (**2g**) (1.42 g., 52%), m.p. 52-53°; nmr (deuteriochloroform: 3.60 δ (s, 3H, N-$CH_3$).

*Anal.* Calcd. for $C_3H_3BrN_4OS$: C, 16.15; H, 1.35; N, 25.12. Found: C, 16.36; H, 1.37; N, 25.00.

2-Methylacetylamino-5-bromo-1,3,4-thiadiazole (**2h**).

Similarly, **1h** (1.92 g.) gave **2h** (1.8 g., 63%), m.p. 129-130° (ligroin); ir: 1678 $cm^{-1}$ (C=O); nmr (deuteriochloroform): 2.45 δ (s, 3H, $COCH_3$), 3.76 δ (s, 3H, N-$CH_3$).

*Anal.* Calcd. for $C_5H_6BrN_3OS$: C, 25.43; H, 2.56; N, 17.80. Found: C, 25.40; H, 2.55; N, 17.95.

2-Methylbenzoylamino-5-bromo-1,3,4-thiadiazole (**2i**).

Compound **1i** (2.68 g.) gave **2i** (3.45 g., 95%), m.p. 179-180° (ethyl acetate); ir: 1637 $cm^{-1}$ (C=O); nmr (deuteriochloroform): 3.70 δ (s, 3H, N-$CH_3$), 7.54 δ (m, 5H, Ar-H).

*Anal.* Calcd. for $C_{10}H_8BrN_3OS$: C, 40.28; H, 2.70; N, 14.09. Found: C, 40.30; H, 2.70; N, 13.90.

Compound **3a** (1.4 g.) gave 1.6 g. of a mixture; tlc analysis showed this to be composed of 2-bromo-4-methyl-5-imino-$\Delta^2$-1,3,4-thiadiazoline (**4a**), 4-methyl-5-bromoimino-$\Delta^2$-1,3,4-thiadiazoline (**3f**) and of 2-bromo-4-methyl-5-bromoimino-$\Delta^2$-1,3,4-thiadiazoline (**4f**). Work up of this mixture with carbon tetrachloride removed **3f**, and the insoluble material (0.8 g.) was a mixture of **4a** and **4f** (tlc); nmr (deuteriochloroform): 3.54 δ (s, 6H, 2x N-$CH_3$), 11.48 δ (br. s, 1H, NH). Crystallization from ethyl acetate gave **4f** (0.35 g., yield 9%), m.p. 142-143°; nmr (deuteriochloroform): 3.56 δ (s, 3H, N-$CH_3$).

*Anal.* Calcd. for $C_3H_3Br_2N_3S$: C, 13.20; H, 1.11; N, 15.39. Found: C, 13.40; H, 0.98; N, 15.28.

The thiadiazoline **4a** could not be isolated; indeed during isolation attempts, it was noticed that it quickly turned into a compound containing bromine, which was insoluble in most organic solvents; investigations are in progress concerning the structure of the latter. From the carbon tetrachloride solution deriving from the mixture work-up above, preparative tlc (silica gel GF 254, cyclohexane-ethyl acetate 2:1) allows one to isolate **4f** (0.15 g.) and **3f** (0.5 g.), m.p. 119° (ligroin); ir: 3030 $cm^{-1}$ (CH); nmr (deuteriochloroform): 3.58 δ (s, 3H, N-$CH_3$), 7.76 δ (s, 1H, CH).

*Anal.* Calcd. for $C_3H_4BrN_3S$: C, 18.57; H, 2.07; N, 21.65. Found: C, 18.50; H, 1.90; N, 21.80.

Acetylation of the **4a**, **4f** and **3f** Mixture.

The mixture (1.6 g.) dissolved in pyridine (10 ml.) and acetic anhydride (1.2 ml.) was heated at reflux for 10 minutes. The solvent and excess acetic anhydride were removed *in vacuo*, the residue was diluted with water and extracted with chloroform.

From the chloroform extract by removal of the solvent, a mixture (1.36 g.) of **3d** and **4d** was obtained which could be isolated by tlc (silica gel GF 254, cyclohexane-ethyl acetate 1:1). Compound **3d** (0.4 g.) showed no melting point depression when mixed with a pure sample obtained by acetylation of **3a** (1,4) and **4d** (0.92 g.) (see below). Carrying out the reaction in the absence of sodium acetate, removal of solvent and treatment with carbon tetrachloride afforded the hydrobromide of **3f** (2.65 g., 69%), m.p. 249-250° (ethanol); nmr (DMSO-$d_6$): 3.81 δ (s, 3H, N-$CH_3$), 8.97 δ (s, 1H, CH), 9.75 δ (br. s, 1H, NH).

*Anal.* Calcd. for $C_3H_4BrN_3S \cdot HBr$: C, 13.10; H, 1.83; N, 15.28. Found: C, 12.85; H, 1.80; N, 15.30.

From the carbon tetrachloride mother liquors one can isolate additional **3f** (0.45 g., 26%).

2-Bromo-4-methyl-5-methylimino-$\Delta^2$-1,3,4-thiadiazoline (**4b**).

Compound **3b** (1.6 g.) gave, after extraction with chloroform, 2.1 g., 82% of **4b**, m.p. 83° (ligroin); nmr (deuteriochloroform): 3.04, 3.54 δ (2s, 6H, 2 x N-$CH_3$).

*Anal.* Calcd. for $C_4H_6BrN_3S$: C, 23.09; H, 2.90; N, 20.19. Found: C, 22.88; H, 2.90; N, 20.25.

Compound **3c** (1.77 g.) likewise gave a crude product (1.5 g.) consisting of **3f** (0.65 g., 30%), which was soluble in carbon tetrachloride and 0.8 g. of starting material, which remained as a residue upon treatment with the above solvent. Following the same general bromination procedure, but doubling the amount of bromine in acetic acid solution employed, one obtained a mixture of **3f** (1.25 g., 52%) and **4f** (0.67 g., 20%), which could be separated by preparative tlc (silica gel GF 254, cyclohexane-ethyl acetate 2:1). Carrying out the reaction in the absence of sodium acetate, the reaction mixture was dissolved in water and neutralized with aqueous sodium bicarbonate, yielding **3f** (2.1 g., 88%).

2-Bromo-4-methyl-5-acetylimino-$\Delta^2$-1,3,4-thiadiazoline (**4d**).

Compound **3d** (1.92 g.) gave, after extraction with chloroform, 2.12 g. of a mixture; preparative tlc (silica gel GF 254 cyclohexane-ethyl acetate 1:1) showed this to be composed by 1.1 g. of starting material and 0.6 g. (yield 20%) of **4d**, m.p. 77-79°; ir: 1608 $cm^{-1}$ (C=O); nmr (deuteriochloroform): 2.31 δ (s, 3H, $COCH_3$), 3.91 δ (s, 3H, N-$CH_3$).

*Anal.* Calcd. for $C_5H_6BrN_3OS$: C, 25.43; H, 2.56; N, 17.80. Found: C, 25.38; H, 2.60; N, 17.65.

2-Bromo-4-methyl-5-benzoylimino-$\Delta^2$-1,3,4-thiadiazoline (**4e**).

Compound **3e** (2.68 g.) gave a crude product (2.40 g.), preparative tlc (silica gel GF 254 cyclohexane-ethyl acetate 7:3) allowed one to isolate 1.62 g. of starting material and 0.6 g. (yield 76%) of **4e**, m.p. 139-141° (ligroin); ir: 1592 $cm^{-1}$ (C=O); nmr (deuteriochloroform): 4.04 δ (s, 3H, N-$CH_3$), 7.27-8.52 δ (m, 5H, Ar-H).

*Anal.* Calcd. for $C_{10}H_8BrN_3OS$: C, 40.28; H, 2.70; N, 14.09. Found: C, 40.30; H, 2.75; N, 13.90.

Methylation of **2a-e** (**4a**•HI).

Compound **2a** (1.8 g., 0.01 mole) in anhydrous methanol (40 ml.) and methyl iodide (0.035 mole) were heated at reflux for 24 hours. After concentration (under reduced pressure) and filtration, the residue was washed with methanol-ligroin, and **4a**•HI (2.7 g., 88%), m.p. 238-241° (water) was obtained.

*Anal.* Calcd. for $C_3H_4BrN_3S \cdot HI$: C, 11.19; H, 1.56; N, 13.05. Found: C, 10.95; H, 1.60; N, 12.98.

Compound **2b** (1.95 g., 0.01 mole) following the procedure above gave **4b**•HI (2.8 g., yield 87%), m.p. 210-212° (water).

*Anal.* Calcd. for $C_4H_6BrN_3S \cdot HI$: C, 14.30; H, 2.10; N, 12.51. Found: C, 14.40; H, 2.10; N, 12.65.

Compound **4b**•HI suspended in a little water and treated with diluted ammonia gave **4b**.

Compound **2c** (0.5 g., 0.0025 mole) suspended in dioxane (25 ml.) was treated with an ethereal solution of diazomethane. After filtration and removal of the solvents, the residue gave, in very poor yield, a mixture of **2g** and **4c** (preparative tlc silica gel GF 254 cyclohexane-ethyl acetate 2:1).

Compound **2d** (2.22 g., 0.01 mole) dissolved in dioxane (120 ml.) and methanol (75 ml.) was treated as above with diazomethane. After removal of the solvents the residue, chromatographed on a dry column of silica gel GF 254 (cyclohexane-ethyl acetate 1:1), gave **4d** (1.65 g., 70%) and **2h** (0.65 g., 27%).

Compound **2e** (2.85 g., 0.01 mole) in dioxane (120 ml.) following the procedure above (eluent: benzene-cyclohexane 4:1) gave **4e** (2.4 g., 64%) and **2i** (0.5 g., 13%).

Compound **4a**•HI (1.6 g., 0.005 mole) was suspended in anhydrous methanol (20 ml.) and a methanolic solution of sodium methoxide (0.3 g. of sodium in 20 ml. of methanol) and dimethyl sulphate (0.5 ml.) were added. The reaction mixture was refluxed for 1 hour, the solvent distilled off, the residue diluted with water and extracted with chloroform leaving **4b** (0.12 g., 11%).

Acetylation of **2a-e**, **3f**, **4a**•HI and **4f**. General Procedure.

The heterocyclic compound (0.005 mole), dissolved or suspended in 5 ml. of pyridine and 0.01 mole of acetic anhydride, were refluxed for 30 minutes. Upon dilution with water, the crude product precipitated out, or it could be extracted with a suitable organic solvent. The following compounds were obtained.

Compound **2a** (0.9 g.) gave **2d** (1 g., 90%).

Compound **2b** (1 g.) gave **2h** (0.82 g., 69%).

Compound **2c** (1.05 g.) gave **2d** (0.3 g., 27%).

Compound **2e** (1.42 g.) gave **2d** (0.62 g., 56%).

Compound **3f** (0.97 g.) gave, after extraction with boiling ligroin, **3d** (0.55 g., 57%).

Compound **4f** (1.37 g.) gave, after extraction with boiling ligroin, **4d** (0.90 g., 76%).

Compound **4a**•HI (1.6 g.) gave, after extraction with chloroform, **4d** (0.9 g., 76%).

Compound **2d**, under the same experimental conditions, was recovered unchanged.

Benzoylation of **2a-e** and **4a**•HI. General Procedure.

The heterocyclic compound (0.005 mole) in pyridine (5 ml.) was refluxed for 15 minutes with benzoyl chloride (0.006 mole). After dilution with water, following the procedure above, the following were obtained.

Compound **2a** gave **2e** (1.1 g., 77%).

Compound **2b** gave **2i** (0.96 g., 64%).

Compound **4a**•HI gave **4e** (0.78 g., 51%).

Under the same experimental conditions **2c**, **2d** and **2e** decomposed.

Nitrosation of **2a-e** and **4a**•HI. General Procedure.

To a suspension or solution of the compound (0.005 mole) dilute hydrochloric acid 1:1 was added aqueous sodium nitrite (0.4 g.). The following compounds were obtained.

Compound **2a** gave **2c** (0.78 g., 75%).

Compound **2b** gave, after extraction with chloroform, **2g** (1 g., 90%).

Compounds **2c**, **2d** and **2e** were recovered unchanged.

2-Bromo-4-methyl-5-nitrosoimino-$\Delta^2$-1,3,4-thiadiazoline (**4c**).

From **4a**•HI without hydrochloric acid, 0.95 g. (85%) of **4c**, m.p. 127° (benzene-ligroin) was obtained; nmr (deuteriochloroform): 4.18 δ (s, 3H, N-$CH_3$).

*Anal.* Calcd. for $C_3H_3BrN_4OS$: C, 16.15; H, 1.35; N, 25.12. Found: C, 16.10; H, 1.38; N, 25.25.

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