4-Bromo-5-methyl-(2*H*)-1,2,6-thiadiazin-3(6*H*)one 1,1-Dioxides

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The title compounds, bearing an alkyl and/or bromine substituent on nitrogen, were synthesized. Unlike 5-bromo-6-methyluracil, 4-bromo-5-methyl-(2*H*)-1,2,6-thiadiazin-3-(6*H*)one 1,1-dioxides have the ability to act as a bromonium ion source.

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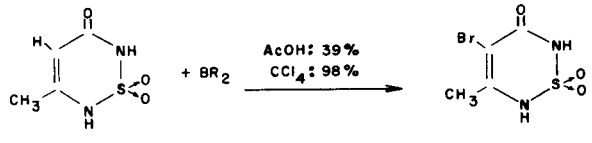
The sulfamoyl group as a substituent on an aromatic or heterocyclic ring, or as a part of a heterocyclic ring system, has been recognized of value, as, for example, in 3,5-dinitrosulfanilamide (1,2), acylated and carbamoylated 2-aminothiazole (3) and 1,3,4-thiadiazole (4), and 1*H*-2,1,3-benzothiadiazine-4-(3*H*)one 2,2-dioxide (5a) herbicides. Since the ureido group is of great importance in cyclic structures acting as herbicides, such as 3-alkyl-5-bromo-6-methyluracils (5b), it was of interest to explore the significance of the sulfamido group in the isosteric thiadiazine ring.

Bromination of 5-methyl-(2*H*)-1,2,6-thiadiazin-3-(6*H*)one 1,1-dioxide (6), **1**, proceeded smoothly with one molar equivalent of bromine in glacial acetic acid at ambient temperature or with a three molar excess of bromine in refluxing carbon tetrachloride to give the 4-bromo derivative, **2**.



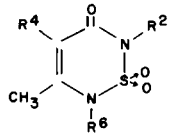
1 2

The low R_F values in both non-planar and polar solvents, and the ability to dissolve in aqueous sodium bicarbonate (carbon dioxide evolution) are indicative of the pronounced anionic character of **2**. The infrared spectrum shows characteristic bands at ν NH 3400-2700, ν C=O 1655, ν C=C 1600, and ν SO_2 1180 and 1350 cm^{-1}. The ^1H nmr spectrum (DMSO-d_6) is simple, showing the expected proton count and shifts of a three-proton singlet at δ 2.3 (CH_3) and two NH protons at 12.2 ppm. Furthermore, the one-proton singlet at δ 5.4 (CH=) of **1** is not apparent in **2**, thereby eliminating from consideration *N*-bromo derivatives of **1**.

In the electron-impact mass spectrum of **2**, the molecular ion is observed at m/e 240, 242 (M^+), indicative of the presence in the molecule of one bromine atom. The characteristic feature of **2** is the bromine attached to the 4-carbon atom such that upon electron impact cyanic acid (m/e 42, base peak) is eliminated to give the prominent ion m/e 197, 199 (path **a**). The ion at m/e 133, 135 is produced from m/e 197, 199 ion by elimination of sulfur dioxide (m/e 64) and on further impact either loses hydrogen bromide (m/e 80,82) to give the ion at m/e 54, or fragments to give cyanogen bromide (m/e 106,108) and ethylene (m/e 28). A second pathway (**b**) which has been observed also involves the initial loss of the bromine atom from the molecular ion

Table

5-Methyl-(2*H*)-1,2,6-thiadiazin-3-(6*H*)one 1,1 Dioxides



Compound	R^2	R^4	R^6	% Yield	Mp., °C	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Bromine (d) Calcd.	Bromine (d) Found	Br^+ Found
1	H	H	H	62	173-175	29.6	29.2	3.7	3.7	17.1	17.2	—	—	—
2	H	Br	H	39 (a)	179-180	19.9	19.7	2.1	1.8	11.6	11.9	33.2	33.3	33.6
2	H	Br	H	98 (b)	179-180	19.9	19.7	2.1	1.9	11.6	11.7	33.2	33.6	33.6
5a,b	C_4H_9	H	H	64-94	(c)	44.0	43.5	6.4	6.9	12.8	12.6	—	—	—
6a,b	C_4H_9	Br	H	98	(c)	32.3	32.1	4.4	4.6	9.4	9.4	26.9	27.0	—
7a,b	C_4H_9	Br	Br	100	(c)	25.5	24.0	3.2	3.0	7.4	7.1	42.6	43.0	—
8a,b	C_4H_9	Br	CH_3	94	(c)	34.7	34.3	4.8	5.0	9.0	9.1	—	—	—

(a) In glacial acetic acid. (b) In carbon tetrachloride. (c) Amber syrup. (d) Average value of 4 analyses.

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to give ion m/e 162.

An unexpected and at first surprising feature of **2** is its tendency to undergo electrophilic substitution in that bromine is eliminated in the cationic (Br^+) form. For example, the total bromine content of **2** can be determined iodometrically (7). In contrast, less than 3% of the total bromine content of 5-bromo-6-methyluracil, which is isosteric with **2**, is available in cationic form.

The reaction of *n*-butylsulfamide (10) with diketene in glacial acetic acid in the presence of mercuric cyanide proceeded somewhat differently from that reported (11). The reaction product, an amber syrup, which showed no tendency to crystallize (lit. (11) m.p. 109-110°) and appeared uniform by thin-layer chromatography, is shown to be a mixture consisting of 60% of 2-butyl-5-methyl-(2*H*)-1,2,6-thiadiazine-3-(6*H*)one 1,1-dioxide, **5a** (δ CH_3 = 2.15), and 40% of positional isomer **5b** (δ CH_3 = 2.30) by ^1H nmr spectral analysis. The mass spectrum obtained on electron impact shows the molecular ion m/e 218 (M^+). The formation of the two positional isomers is rationalized on the basis that acyl bond cleavage by *n*-butylsulfamide of diketene involves both the nitrogen atom carrying the butyl group (to give **3** → **5a**) and the NH_2 group (to give **4** → **5b**).

Bromination of the mixture, **5a** and **5b**, in glacial acetic acid gave impure products. In carbon tetrachloride, the mixture reacted readily with one molar equivalent of bromine to give the isomeric mixture, **6a** and **6b**, in almost quantitative yield. Again, two lines for the 5-methyl group in the ^1H nmr spectrum indicate a 3:2 mixture: **6a** (δ CH_3 = 2.35), **6b** (δ CH_3 = 2.55), the *n*-butyl group residing on either nitrogen atom. Because of its strong anionic characteristics, **6a,b** dissolves in aqueous sodium bicarbonate. Acidification of this solution with hydrochloric acid liberates **6a,b**, which is soluble in ether.

When the 3:2 mixture, **5a** and **5b**, was allowed to react with two molar equivalents of bromine in refluxing carbon tetrachloride, the dibrominated product, **7a** and **7b**, was obtained in quantitative yield.

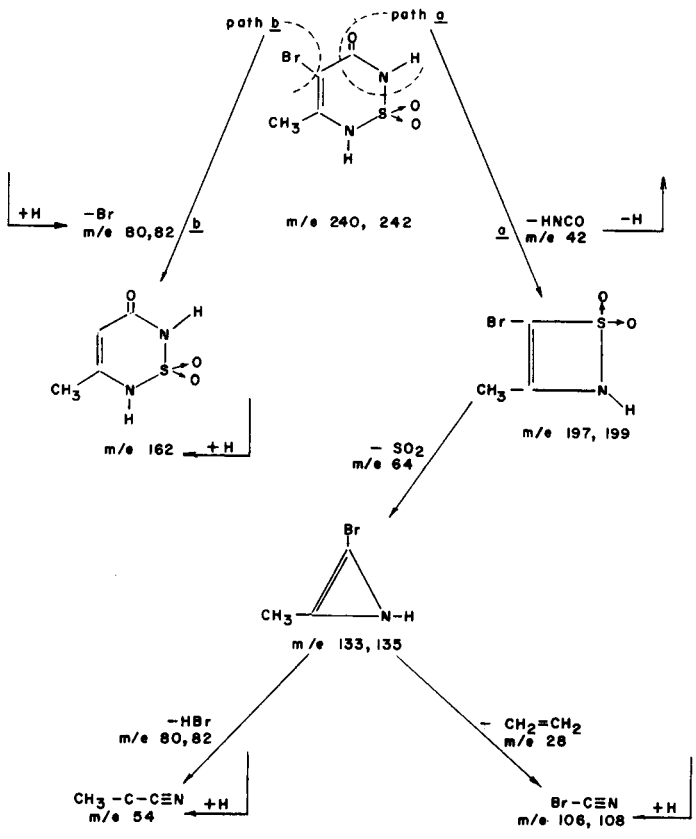
The mixture **6a** and **6b**, reacted readily with ethereal diazomethane to **8a** (δ CH_3 = 2.4) and **8b** (δ CH_3 = 2.85) in 94% yield. The infrared spectrum shows strong carbonyl (ν 1690) and ν SO_2 1350 and 1180 cm^{-1} absorption bands.

Of the brominated compounds listed in the Table, none showed herbicidal activity. This corroborates recent findings with closely related 1,2,6-thiadiazinone 1,1-dioxides (12). In explanation, we suggest that the tendency of the 4-brominated members of this ring system to act as brominating (oxidizing) agents may account for their inactivity.

EXPERIMENTAL

4-Bromo-5-methyl-2*H*-1,2,6-thiadiazin-3-(6*H*)one 1,1-Dioxide **2**.

MASS SPECTRAL FRAGMENTATION PATTERN OF 2



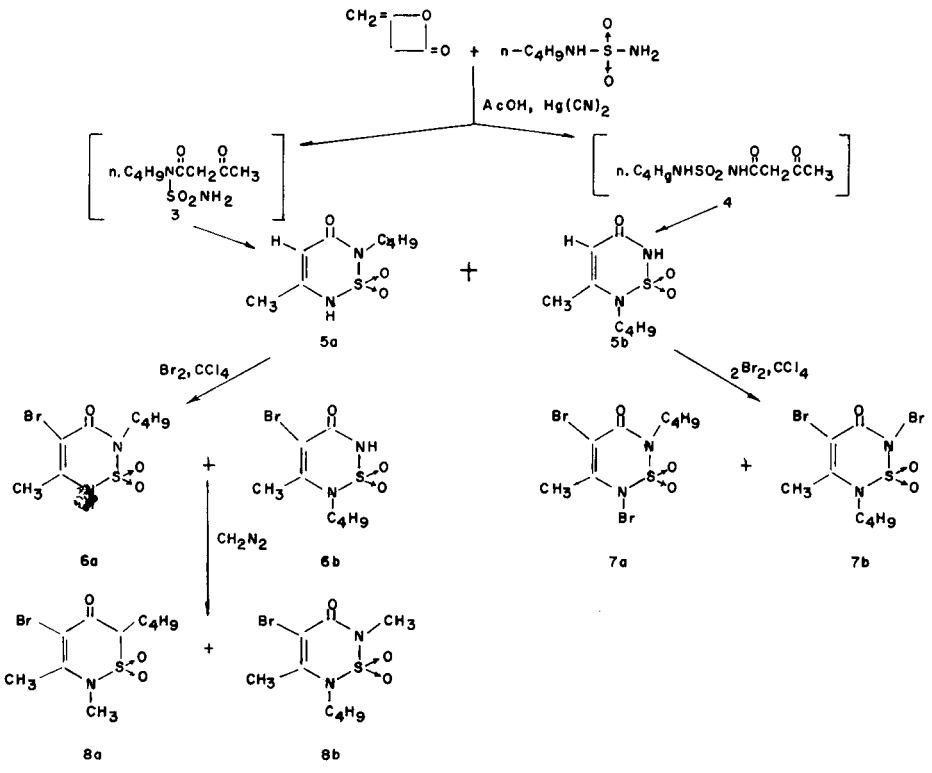
To a warm (45°) and stirred mixture of 32.4 g. (0.2 mole) of **1** in 250 ml. of carbon tetrachloride was added dropwise 96 g. (0.6 mole) of bromine. The mixture was subsequently refluxed for 2 hours. After 18 hours at ambient temperature, the solid was removed by filtration. Recrystallization from nitromethane gave 47 g. (98%) of **2**, a cream colored solid, m.p. 179-180°.

2-(and 6)-Butyl-5-methyl-2*H*-1,2,6-thiadiazin-3-(6*H*)one 1,1-Dioxide, **5a** + **5b**.

A stirred mixture containing 30.4 g. (0.2 mole) of *N*-butylsulfamide, 0.8 g. of mercuric cyanide and 32 ml. of freshly distilled diketene in 80 ml. of glacial acetic acid was gradually heated with stirring. At 65-70°, an exothermic reaction caused the temperature to rise rapidly to 110°. After two minutes, the temperature decreased, and the reaction mixture was concentrated on a rotary evaporator. The residual syrup dissolved in ether was charcoaled, passed through celite, and concentrated under reduced pressure (30 mm) at 100° for 48 hours. Thin-layer chromatography showed only one spot at R_f 0.27 (solvent system (by volume: Hexane (2), ethyl acetate (40), tetrahydrofuran (40)). The compound shows no tendency to crystallize, yield, 37 g. (64%), an amber syrup.

4-Bromo-2-(and 6)-butyl-5-methyl-2*H*-1,2,6-thiadiazin-3-(6*H*)one 1,1-Dioxide, **6a** + **6b**.

Bromine, 21.4 g. (0.134 mole), was added dropwise (10 minutes) to a stirred solution of 29.3 g. (0.134 mole) of **5a** + **5b** in 100 ml. of carbon tetrachloride. The temperature was controlled at 25° with an ice bath during this addition. After 30 minutes, the reaction mixture was concentrated to give 38.7 g. (97.5%) of **6a** + **6b**, an amber syrup.



2-(and 6)-Butyl 4,6-(and 2,4)-dibromo-5-methyl-(2*H*)-1,2,6-thiadiazine-3-(6*H*)one, **7a** + **7b**.

Bromine, 60.2 g. (0.376 mole), was added gradually to a solution of 41 g. (0.188 mole) of **5a** + **5b** in 200 ml. of carbon tetrachloride. The reaction mixture was refluxed for 7 hours and concentrated to give 73.7 g. (100%) of **7a** + **7b**, an amber syrup.

4-Bromo-2-(and 6)-butyl-5,6-(and 2,5)-dimethyl-(2*H*)-1,2,6-thiadiazine-3-(6*H*)one 1,1-Dioxide **8a** + **8b**

A solution of 9 g. (0.214 mole) of diazomethane in 500 ml. of ether was added gradually to a solution of 32 g. (0.108 mole) of **6a** + **6b** in 100 ml. of ether. After 18 hours at ambient temperature, ether was removed under reduced pressure. The residual oil, 31.5 g. (94%) of crude **8a** + **8b** was purified by column chromatography to give 5.5 g. of a homogenous (by tlc) material; R_F = 0.29 (in solvent system (by volume): Hexane (80), ethyl acetate (16), tetrahydrofuran (4)).

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(7) The ability of certain polyhalogeno compounds, α-haloketones, α-bromodicarbonyl compounds, α-halosulfones, dinitrohalomethanes, 2,4-dibromo (and diiodo) phenols, phenol ethers and aromatic amines to act as oxidizing or halogenating agents is well documented (8). 5,5-Dibromo-2,2-dimethyl-4,6-dioxo-1,3-dioxane can mono-brominate saturated aldehydes and ketones with excellent yields and the α′-carbon atom of α,β-unsaturated ketones with high selectivity (9).

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