A Facile Preparation of 2,4-Disubstituted 2*H*-1,2,4,6-Thiatriazin-3(4*H*)-one 1,1-Dioxides

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2*H*-1,2,4,6-Thiatriazin-3(4*H*)-one 1,1-dioxides[1] are structural analogues of 1,3,5-triazine-2,4-(1*H*,3*H*)-diones, which are strong inhibitors of photosynthesis in plants[2]. Their syntheses have been intensively studied because of their biological activity[1]. However, these methods involve several steps with low overall yields and are useful only for a limited variety of derivatives[3]. We now present here a novel and facile preparation of 2,4-disubstituted 2*H*-1,2,4,6-thiatriazin-3(4*H*)-one 1,1-dioxides **5** via a two-step process.

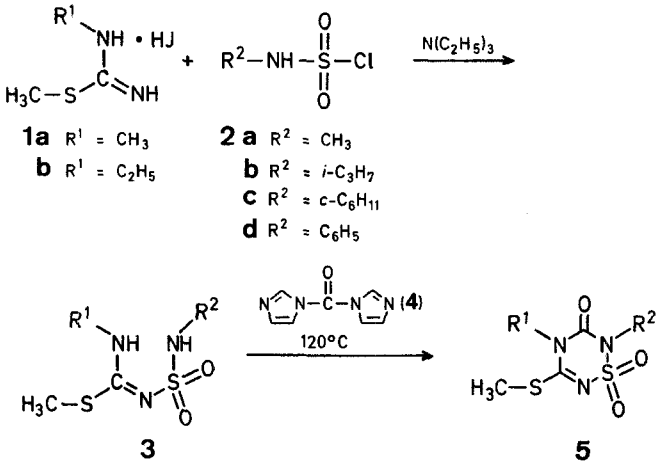

Table 1. 1-Substituted 2-Methyl-3-sulfamoylisothioureas **3** prepared

Product No.	Yield [%]	m.p. [°C]	Molecular Formula[a]	M.S. *m/e* (rel. intens. %)	I.R. (Nujol) ν_{NH} [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
3aa	73	oil	$C_4H_{11}N_3O_2S_2$ (197.2)	197 (M^+, 2); 57 (100)	3570, 3300	2.39 (s, 3H); 2.68 (d, J = 5.4 Hz, 3H); 2.94 (d, J = 5.4 Hz, 3H); 4.69 (q, J = 5.4 Hz, 1H); 7.40–7.88 (broad, 1H)
3ab	51	oil	$C_6H_{15}N_3O_2S_2$ (225.3)	225 (M^+, 12); 57 (100)	3570, 3300	1.19 (d, J = 6.0 Hz, 6H); 2.41 (s, 3H); 2.97 (d, J = 5.4 Hz, 3H); 3.21–3.86 (m, 1H); 4.21–4.50 (broad, 1H); 7.50–7.98 (broad, 1H)
3ac	56	71–74°	$C_9H_{19}N_3O_2S_2$ (265.4)	265 (M^+, 4); 57 (100)	3570, 3290	1.03–2.21 (m, 10H); 2.41 (s, 3H); 2.98 (d, J = 5.4 Hz, 3H); 3.10–3.59 (broad, 1H); 4.47 (d, J = 7.2 Hz, 1H); 7.50–8.05 (broad, 1H)
3ad	69	oil	$C_9H_{13}N_3O_2S_2$ (259.5)	259 (M^+, 5); 57 (100)	3580, 3290	2.28 (s, 3H); 2.90 (d, J = 5.4 Hz, 3H); 6.92–7.20 (broad, 1H); 7.25 (s, 5H); 7.60–8.09 (broad, 1H)
3ba	78	oil	$C_5H_{13}N_3O_2S_2$ (211.3)	211 (M^+, 7); 71 (100)	3580, 3300	1.29 (t, J = 7.0 Hz, 3H); 2.42 (s, 3H); 2.73 (s, 3H); 3.10–3.62 (broad, 2H); 4.20–4.95 (broad, 1H); 7.50–8.10 (broad, 1H)
3bc	62	oil	$C_{10}H_{21}N_3O_2S_2$ (279.4)	279 (M^+, 9); 71 (100)	3570, 3290	1.00–2.20 (m, 10H); 1.20 (t, J = 7.0 Hz, 3H); 2.52 (s, 3H); 2.90–3.55 (broad, 1H), 4.02 (q, J = 7.0 Hz, 2H); 4.50–4.92 (broad, 1H); 7.55–8.10 (broad, 1H)

[a] The microanalyses were in satisfactory agreement with calculated values: C ±0.3; H ±0.3; N ±0.3.

Table 2. 2,4-Disubstituted 5-Methylthio-2*H*-1,2,4,6-thiatriazin-3(4*H*)-one 1,1-Dioxides **5** prepared

Product No.	Yield [%]	m.p. [°C]	Molecular Formular[a] or Lit. m.p. [°C]	M.S. *m/e* (rel. intens. %)	I.R. (Nujol) $\nu_{C=O}$	I.R. (Nujol) ν_{SO_2} [cm^{-1}H	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
5aa	85	92°	$C_5H_9N_3O_3S_2$ (223.3)	223 (M^+, 49); 119 (100)	1710	1330, 1310 1170, 1090	2.57 (s, 3H); 3.34 (s, 3H); 3.44 (s, 3H)
5ab	91	99–100°	99°[3]	251 (M^+, 2); 173 (100); 120 (84); 43 (100)	1715	1330, 1310 1170, 1090	1.51 (d, J = 6.6 Hz, 6H); 2.50 (s, 3H); 3.36 (s, 3H); 4.26–4.83 (m, 1H)
5ac	89	143°	$C_{10}H_{17}N_3O_3S_2$ (291.4)	291 (M^+, 1); 210 (100)	1715	1330, 1310 1180, 1090	1.07–2.23 (m, 10H); 2.51 (s, 3H); 3.36 (s, 3H); 3.79–4.20 (broad, 1H)
5ad	76	204°	$C_{10}H_{11}N_3O_3S_2$ (285.3)	285 (M^+, 71); 119 (100)	1720	1330, 1310 1180, 1090	2.60 (s, 3H); 3.50 (s, 3H); 7.47 (s, 5H)
5ba	82	128–129°	$C_6H_{11}N_3O_3S_2$ (237.3)	237 (M^+, 20); 133 (52); 69 (100)	1710	1330, 1310 1170, 1090	1.31 (t, J = 7.0 Hz, 3H); 2.54 (s, 3H); 3.31 (s, 3H); 3.95 (q, J = 7.0 Hz, 2H)
5bc	67	123–126°	$C_{11}H_{19}N_3O_3S_2$ (305.4)	305 (M^+, 1); 262 (34); 224 (100)	1720	1330, 1310 1180, 1090	1.15–2.40 (m, 10H); 1.32 (t, J = 7.2 Hz, 3H); 2.55 (s, 3H); 3.94 (q, J = 7.2 Hz, 2H); 4.10–4.65 (broad, 1H)

[a] The microanalyses were in satisfactory agreement with calculated values: C ±0.3; H ±0.3; N ±0.3.

The reaction of 1-substituted 2-methylisothioureas **1**[4] with sulfamoyl chlorides **2**[5] in the presence of triethylamine at room temperature gave 1-substituted 2-methyl-3-sulfamoylisothioureas **3** in good yields (Table 1). The structure of **3** was determined on the basis of spectroscopic and analytical data. 3-Sulfamoylation of **1** was suggested by the ^{1}H-N.M.R. spectra of **3aa–3ad** which exhibited a doublet at $\delta = 2.9–3.0$ ppm due to the 1-methyl substituent. One-step cyclization of **3** was easily achieved upon treatment with 1,1′-carbonyldiimidazole **(4)** at 120 °C for 1 h to afford 2,4-disubstituted 5-methylthio-2*H*-1,2,4,6-thiatriazin-3(4*H*)-one 1,1-dioxides **5** in good yields (Table 2). Reaction times longer than 1 h decreased the yields. The cyclic structure of **5** was confirmed by analytical data, ^{1}H-N.M.R., I.R., and mass spectra.

Because of the simple procedure, the good yields, and easy availability of the starting isothioureas **1**, this method provides an attractive synthetic method to 2*H*-1,2,4,6-thiatriazin-3(4*H*)-one 1,1-dioxides **5**.

The melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. I.R. spectra were recorded with a Hitachi 270–30 spectrophotometer. ^{1}H-N.M.R. spectra were determined on a Hitachi R-24B (60 MHz) spectrometer. Electron impact mass spectra were measured with a Hitachi M-80 spectrometer using an ionizing energy of 70 eV.

1-Substituted 2-Methyl-3-sulfamoylisothioureas 3; General Procedure:

To a solution containing 1-substituted 2-methylisothiourea hydroiodide **1**[4] (10 mmol) and triethylamine (2.53 g, 25 mmol) in anhydrous acetonitrile (200 ml) is added dropwise sulfamoyl chloride **2**[5] (12 mmol) in acetonitrile (10 ml) at −30 °C under a nitrogen flow. The mixture is allowed to warm to room temperature, stirred overnight, and concentrated under reduced pressure. After adding water (200 ml) to the residual mixture, the product is extracted with chloroform (2 × 100 ml). The combined chloroform extract is dried with magnesium sulfate and evaporated to dryness. The residue is chromatographed on a silica gel column using hexane/ethyl acetate (1:1) as eluent to give **3** as a colorless oil (Table 1).

2,4-Disubstituted 3-Methylthio-2*H*-1,2,4,6-thiatriazin-3(4*H*)-one 1,1-Dioxide 5; General Procedure:

A mixture of 1-substituted 2-methyl-3-sulfamoylisothiourea **3** (2 mmol) and 1,1′-carbonyldiimidazole (**4**; 0.65 g, 4 mmol) is stirred at 120 °C for 1 h and the product formed is isolated by short column chromatography on silica gel using hexane/acetone (4:1) as eluent. Subsequent recrystallization from isopropanol/hexane affords colorless crystals of **5** (Table 2).

Received: February 29, 1984

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