A Convenient Synthesis of 5-Alkyl- and 5-Aryl-1,2,3,4-thiatriazoles

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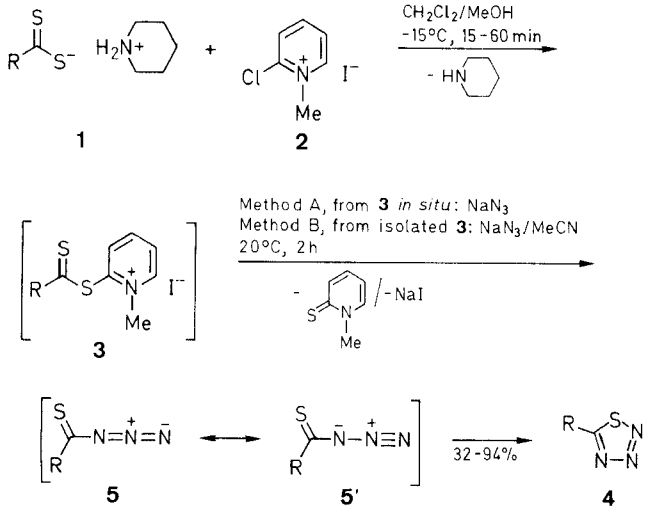
1-Methyl-2-thioacylthiopyridinium salts react with sodium azide to afford 5-alkyl- and 5-aryl-1,2,3,4-thiatriazoles in good yields.

Since the first synthesis of 5-phenyl-1,2,3,4-thiatriazole in 1896,[1] a number of 5-aryl-1,2,3,4-thiatriazoles **4** (R = aryl) have been synthesized.[2,3] On the other hand, the isolation of only one 5-alkyl-1,2,3,4- **4** (R = alkyl), a 5-benzyl derivative,[4,5] has been described due to their instability and difficulties in obtaining the required starting compounds such as aliphatic thioacyl chlorides and hydrazides. We now report a convenient synthesis of 5-alkyl and aryl-1,2,3,4-thiatriazoles **4**.



4	R	4	R	4	R
a	Me	**f**	cyclohexyl	**k**	4-$MeOC_6H_4$
b	Et	**g**	Ph	**l**	4-ClC_6H_4
c	Pr	**h**	2-MeC_6H_4	**m**	1-naphthyl
d	*i*-Pr	**i**	4-MeC_6H_4		
e	Bu	**j**	2,4,6-$Me_3C_6H_2$		

The synthesis of the thiatriazoles **4** was achieved by the use of 1-methyl-2-thioacylthiopyridinium salts[6] **3** as thioacylating agents.

The synthesis of thiatriazoles **4** is either performed as a one-pot reaction in which sodium azide is added to the reaction mixture of the preparation of the 1-methyl-2-thioacylthiopyridinium iodide **3** from a piperdinium dithiocarboxylate[7] **1** and 2-chloro-1-methylpyridinium iodide **(2)** in dichloromethane/methanol (Method A), or a suspension of sodium azide in acetonitrile is added to a solution of the pyridinium salt **3** in acetonitrile (Method B).

The present reaction is assumed to proceed through the intermediate, thioacyl azides **5** as intermediates which are formed by attack of azide anion on the thiocarbonyl C-atom of **3**.

The procedures used for the preparation of compounds **4** are simple and the yields are high. In addition, the starting compounds **1** and **2** are readily available.

5-Alkyl- and 5-Aryl-1,2,3,4-thiatriazoles 4; Typical Procedures:

Method A, without Isolation of Pyridinium Salts **3**:

5-Ethyl-1,2,3,4-thiatriazole **(4b)**: A solution of piperidinium ethanecarbodithioate (**1b**; 280 mg, 1.5 mmol) in CH_2Cl_2 (20 mL) is added dropwise to a stirred solution of 2-chloro-1-methylpyridinium iodide (**2**; 402 mg, 1.5 mmol) in CH_2Cl_2/MeOH (5:1; 10 mL) and the mixture is stirred at −15°C for 15 min. To the resultant mixture containing 2-[ethyl(thiocarbonylthio)]-1-methylpyridinium iodide **(3b)** is added NaN_3 (204 mg, 3 mmol), and stirring is continued at 20°C for 2 h. The solvent is removed under reduced pressure and CH_2Cl_2 (30 mL) is added. The mixture is washed with water (2 × 40 mL), dried (Na_2SO_4), and evaporated using a rotary evaporator. The residue is purified by preparative TLC on silica gel [CH_2Cl_2/hexane (1:2)] to give **4b** as a slightly yellow oil; yield: 110 mg (73%); R_f 0.25.

Method B, from the Isolated Pyridinium Salts **3**:

5-(4-Methylphenyl)-1,2,3,4-thiatriazole **(4i)**: A solution of 1-methyl-2-[4-methylphenyl(thiocarbonylthio)]pyridinium iodide[6] (**3i**; 194 mg, 0.5 mmol) in MeCN (20 mL) is added to a suspension

Table. 5-Alkyl- and 5-Aryl-1,2,3,4-thiatriazoles **4** Prepared

Product	Method[a]	Yield[b] (%)	mp (°C)	Molecular Formula[c] or Lit. mp (°C)	MS (20 eV)[d] *m/z* (%)	IR[e] $\nu_{C=S}$ (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ	^{13}C-NMR ($CDCl_3$/TMS) δ
4a	A	73	oil	$C_2H_3N_3S$ (101.1)	101 (M^+, 10), 73 (61)	1200	3.01 (s, 3H, CH_3)	12.7 (CH_3), 175.9 (C=N)
4b	A	68	oil	$C_3H_5N_3S$ (115.1)	115 (M^+, 30), 87 (82), 55 (25)	1190	1.54 (t, 3H, CH_3), 3.36 (q, 2H, CH_2)	14.3 (CH_3), 21.3 (CH_2), 182.9 (C=N)
4c	A	85	oil	$C_4H_7N_3S$ (129.1)	129 (M^+, 51), 69 (54)	1180	1.08 (t, 3H, CH_3), 1.93 (m, 2H, CH_2), 3.31 (t, 2H, CH_2)	13.5 (CH_3), 23.4 (CH_2), 29.3 (CH_2)
4d	A	79	oil	$C_5H_9N_3S$ (129.1)	130 (M^+, 9), 128 (42), 69 (11)	1205	1.66 (d, 6H, CH_3), 3.73 (m, 1H, CH)	23.4 (CH_3), 29.0 (CH), 188.1 (C=N)
4e	A	83	oil	$C_5H_9N_3S$ (143.1)	143 (M^+, 9), 83 (78)	1230	0.99 (t, 3H, CH_3), 1.48 (m, 2H, CH_2), 1.89 (m, 2H, CH_2), 3.33 (t, 2H, CH_2)	13.5 (CH_3), 22.1, 27.1, 32.0 (CH_2), 181.5 (C=N)
4f	A	79	oil	$C_7H_{11}N_3S$ (169.1)	170 (M^+, 9), 110 (100)	1200	1.5~2.2 (m, 10H, CH_2), 3.39 (m, 1H, CH)	25.4, 25.7, 34.1 (CH_2), 37.9 (CH), 187.0 (C=N)
4g	B	94	94–96	95–96[5]	163 (M^+, 11), 135 (24), 103 (44)	1240	7.5–8.1 (H_{arom})	126.4, 129.7, 129.9, 133.2 (C_{arom}), 179.2 (C=N)
4h	B	74	45–47	45–46[5]	149 (11)	1290	2.62 (CH_3), 7.4–8.0 (H_{arom})	21.9 (CH_3), 125.9, 126.9, 131.2, 132.0, 137.9 (C_{arom}), 177.6 (C=N)
4i	B	76	98–100	98–99[5]	177 (M^+, 16), 149 (2), 117 (76)	1240	2.45 (CH_3), 7.3–7.9 (H_{arom})	21.6 (CH_3), 123.6, 129.6, 130.4, 144.1 (C_{arom}), 179.2 (C=N)
4j	B	32	58–61	$C_{10}H_{11}N_3S$ (205.1)	177 (2), 145 (11)	1240	2.09 (CH_3), 2.36 (CH_3), 7.01 (H_{arom})	20.5, 20.6, 21.2 (CH_3), 128.2, 129.1, 137.2, 141.0 (C_{arom}), 177.0 (C=N)
4k	B	82	105–107	103–104[5]	193 (M^+, 14), 164 (36), 150 (100), 133 (87)	1240	3.90 (CH_3), 7.0–8.0 (H_{arom})	55.6 (CH_3O), 115.1, 118.9, 131.5, 163.5 (C_{arom}), 178.7 (C=N)
4l	B	80	102–103	101–102[5]	199 (M^+, 2), 197 (M^+, 5), 169 (90), 137 (100)	1235	7.5~8.0 (H_{arom})	124.8, 130.1, 139.5 (C_{arom}), 177.9 (C=N)
4m	B	73	46–47	47–48[5]	214 ($M^+ + 1$, 25)[e], 186 (100), 154 (72)	1240	7.5~8.6 (H_{arom})	123.0, 124.7, 125.1, 127.1, 128.5, 128.9, 130.0, 131.4, 133.3, 133.9 (C_{arom}), 178.1 (C=N)

[a] Method A: molecular ratio **3**/NaN_3 = 1:2; CH_2Cl_2/MeOH = 5:1, 20°C, 2 h.
Method B: Molecular ratio **3**/NaN_3 = 0.5:1.2; MeCN, 82°C, 2 h.
[b] Yield is isolated product.
[c] Satisfactory microanalyses: C ±0.19, H ±0.15. Satisfactory HRMS: ±0.0028.
[d] EI method.
[e] Neat for 5-alkyl derivatives (**4a–f**) and KBr for 5-aryl derivatives (**4g–m**).

of NaN_3 (75 mg, 1.1 mmol) in MeCN (10 mL), and the mixture is stirred at 30°C for 2 h. The solvent is evaporated under reduced pressure, CH_2Cl_2 (20 mL) is added, and the solution is washed with water (2 × 40 mL) and dried (Na_2SO_4). Evaporation of CH_2Cl_2 using a rotary evaporator, followed by TLC of the residue in silica gel [CH_2Cl_2/hexane (1:2)] affords **4i** as slightly yellow crystals; yield: 67 mg (76%); R_f 0.35.

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