

2,4-Diamino-1,3-thiazole Hydrotribromide; A New Brominating Agent

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



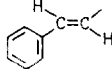
There is continued interest in new solid, selective brominating agents^{1,2,3}.

When bromine is added dropwise to an aqueous or acetic acid solution of 2,4-diamino-1,3-thiazole hydrobromide⁴ (**1a**) in the presence of hydrogen bromide, decolorization takes place and after 1–2 h, a pale yellow solid precipitates. This bromination reaction differs from a previously reported halogenation of 2-amino-1,3-thiazoles⁵ in that the brominated 2,4-diamino-1,3-thiazole described here contains 1 equiv of “free” bromine (KJ titration). Formula **2a** may be assigned to the bromination product. The same reaction occurs when 4-amino-2-dimethylamino-1,3-thiazole hydrobromide (**1b**) is treated with bromine.

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







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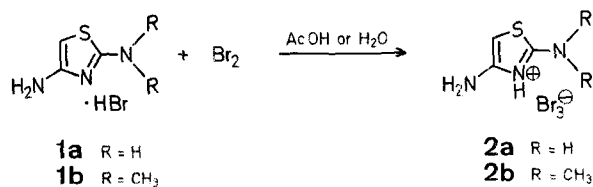
Table 1. 1-Bromoalkyl Ketones (4) from Methylene Ketones (3)

4	R ¹	R ²	Brominating Agent	Yield ^a [%]	m.p. or b.p./torr [°C]		Purity ^b [%], Remarks
					found	reported	
a		H	2a	90	b.p. 140–142°/15 torr	b.p. 133–135°/12 torr ⁶	95
			2b	85			
b		H	2a	97	m.p. 98–99°	m.p. 98° ⁷	95
c		H	2a	90	b.p. 230–234°/15 torr	b.p. 225–230°/12 torr ⁸	95
d		CH ₃	2a	80	b.p. 129–133°/15 torr	b.p. 134–135°/18 torr ⁹	90
e		H	2a	65 ^c	m.p. 44–45°	m.p. 45–46° ³	95 ^d
			2b	60 ^c			

^a Yield of isolated product.^b Determined by G.L.C. analysis for liquid products and by T.L.C. analysis for solid products, and by ¹H.N.M.R. analysis.^c After purification of the crude product by column chromatography on silica gel using ether/light petroleum (2/1) as eluent.^d Bromination of benzylidenacetone³ (3e) with 2a takes place mainly at the methyl group, contrary to the bromination with elemental bromine. Bromination of the C = C group occurs to only ~ 10 %.

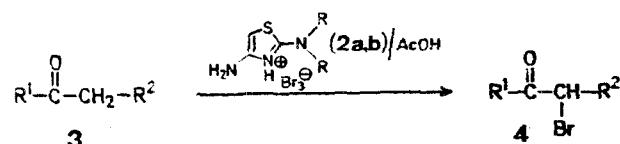
Table 2. Bromophenols (6) from Phenols (5)

Phenol	Bromo-phenol	Brominating Agent	Yield ^a [%]	m.p. or b.p./torr [°C]		Remarks
				found	reported	
 5a	 6a	2a	83	(20)	— ^b	b.p. 195–200°/760 torr ¹⁴ m.p. 64° ¹³
	 6a'			(80)	— ^b	
 5b	 6b	2a	98 ^c	(3)	— ^b	m.p. 46–47° ¹² m.p. 128° ¹¹
	 6b'			(97)	m.p. 127–128°	
 5c	 6c	2a	82	m.p. 79–81°	m.p. 81–82° ¹⁰	6b may be removed by recrystallization from petroleum ether pure according to T.L.C. and G.L.C. analysis

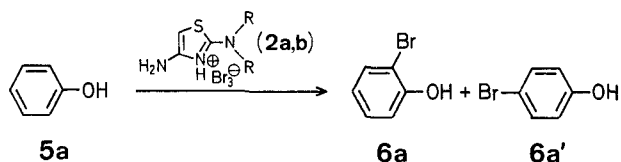
^a Yield of isolated product.^b Not isolated; the relative amounts were determined (by G.L.C. analysis) by comparison with authentic samples.^c Bromination of 1-naphthol (5b) with elemental bromine affords a mixture of mono- and dibrominated products. 4-Bromo-1-naphthol (6b') may also be prepared by reaction of bis [1-naphthyl] carbonate (from 1-naphthol and phosgene) with bromine and subsequent hydrolysis of the bis [4-bromo-1-naphthyl]-carbonate¹¹.

Products 2a, b are stable in the dark for several weeks. I checked the applicability of these compounds as brominating agents and found that aryl and styryl methylene ke-

tones (3) are brominated by 2a, b in acetic acid (reaction time: 1–2 days) to give the corresponding 1-bromoalkyl ketones (4) in high yields.



Likewise, phenols (5) are monobrominated by 2a, b to give bromophenols (6).



In the solvents used, compounds **1a, b** which are formed in the reaction are only poorly soluble so that they can be easily recovered by simple filtration after each run. When methanol, in which compounds **1a, b** and **2a, b** are soluble, is used as solvent the reactions proceed faster (few hours) than in acetic acid but the yields of monobromination products are unsatisfactory and tars are also formed.

From the results reported here it can be seen that the new reagents **2a** and **2b** represent a useful complement to the known solid brominating agents.

Melting and boiling points are uncorrected. T.L.C. analyses were carried out on silica gel using benzene/light petroleum (3/1) or ether/light petroleum (2/1) as eluents. G.L.C. analyses were carried out using a Hewlett-Packard instrument (1 m SE 30, Chromosorb W). ¹H-N.M.R. spectra were recorded on a Varian 60 MHz spectrophotometer.

2,4-Diamino-1,3-thiazole Hydrotribromide (2a):

To a solution of 2,4-diamino-1,3-thiazole hydrobromide (**1a**; 11.7 g, 0.0597 mol) in acetic acid (90 ml) or water (90 ml), 48% hydrobromic acid (12.5 ml) is slowly added. Bromine (3 ml, slightly less than 1 equiv) is then added dropwise to the vigorously stirred mixture at 0°C. After 1–2 h, the solid product **2a** precipitates. It is isolated by suction and washed with ether or chloroform; yield: 18 g (85%). The product is recrystallized (without heating) from a small amount of methanol; yield of pure **2a**: 13 g (60%); m.p. 198–200°C (dec.).

$\text{C}_3\text{H}_6\text{Br}_3\text{N}_3\text{S}$	calc.	C 10.12	H 1.70	N 11.81
(355.8)	found	10.00	1.85	11.71

4-Amino-2-dimethylamino-1,3-thiazole Hydrotribromide (2b)

is prepared in the same manner; yield: 80%; m.p. 150–153°C (dec.).

$\text{C}_5\text{H}_{10}\text{Br}_3\text{N}_3\text{S}$	calc.	C 15.64	H 2.63	N 10.94
(383.9)	found	15.50	2.84	10.73

The ¹H-N.M.R. spectra of **2a, b** in DMSO-*d*₆ are identical with the spectra of **1a, b** in the same solvent⁴. It may be assumed that the debromination of **2a, b** proceeds rapidly in the presence of a large excess of dimethyl sulfoxide. The same behaviour is observed in acetone-*d*₆. The use of solvents such as methanol-*d*₄ and D₂O for recording of the ¹H-N.M.R. spectra leads to fast H/D exchange at C-5 of the 1,3-thiazole ring⁴.

General Bromination Procedure:

The hydrotribromide **2a** or **2b** (0.02 mol) is added to a vigorously stirred solution of the substrate (0.02 mol) in acetic acid (40 ml) at room temperature. The progress of the bromination is followed by T.L.C. [silica gel, eluent: ether/light petroleum 2/1 (for ketones; reaction time: 1–2 d) or chloroform (for phenols; reaction time: ~1 d)]. When no more starting material (ketone or phenol) is present the hydrobromide **1a, b** is recovered by filtration. The filtrate is poured onto ice (100 g) and (only in the case of ketones) the mixture is neutralized with sodium hydrogen carbonate. The mixture is extracted with ether (5 × 20 ml), the extract is dried with sodium sulfate and evaporated, and the residual product is purified by recrystallization or distillation *in vacuo*.

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⁴ Compounds **1a** and **1b** can be easily prepared by intermolecular cyclocondensation of thiourea (or *N,N*-dimethylthiourea) with chloroacetonitrile:

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