

**1,2,4-Triazines. I. A Convenient Synthesis of
4,5-Dihydro-1,2,4-triazin-3-(2H)one and its 6-Substituted Derivatives**
Yoshinori Nakayama, Yuzuru Sanemitsu (1), Masato Mizutani and Hirosuke Yoshioka

Pesticide Division, Institute for Biological Science, Sumitomo Chemical Co. Ltd.,
Takarazuka, Hyogo 665, Japan
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A facile synthesis of 4,5-dihydro-1,2,4-triazin-3-(2H)one (**2a**) from 5-methylthio-1,2,4-triazin-3-(2H)one (**1a**) with sodium borohydride is described. The reaction provides a convenient method for its 6-substituted derivatives (**2b-h**).

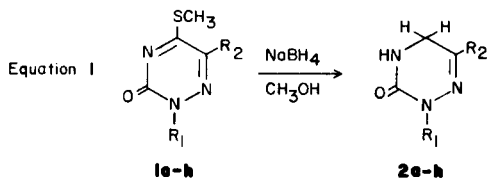
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Although several methods for syntheses of 4,5-dihydro-1,2,4-triazin-3-(2H)one and its 6-substituted derivatives from different starting materials have been reported (2), they involve many steps with low overall yields and limited variety of derivatives.

We wish to report a facile route to 4,5-dihydro-1,2,4-triazin-3-(2H)one **2a** and its 6-substituted derivatives **2b-h**. They were prepared by the reduction with sodium borohydride of 5-methylthio-1,2,4-triazin-3-(2H)one derivatives **1a-h** which were easily obtained from thio-

Table 1

Synthesis of 4,5-Dihydro-1,2,4-triazin-3-(2H)one Derivatives



Compound No.	R ₁	R ₂	Yield (%)	M.p. (°C)	Pmr Spectral Data (δ)			
					2-NR ₁	4-NH	5-CH ₂	6-R ₂
2a	H	H	70.6	135-136 (a)	9.55 (br)	6.90 (br)	3.86 (t)	6.80 (t)
2b	H	CH ₃	88.4	147-148 (b)	9.29 (br)	6.86 (br)	3.74 (d)	1.82 (s)
2c	H	CH(CH ₃) ₂	73.6	156-157	9.36 (br)	6.94 (br)	3.75 (d)	1.02 (d) 2.45 (m)
2d	H	C ₆ H ₁₁	69.0	172-173	9.25 (br)	6.83 (br)	3.27 (d)	1.1-1.8 (m) 2.0-2.4 (m)
2e	H	C ₆ H ₅	68.5	225-226 (c)	9.96 (br)	7.27 (br)	4.29 (d)	7.4-7.7 (m)
2f	CH ₃	H	82.5	103-104	3.11 (s)	6.86 (br)	3.71 (t)	6.91 (t)
2g	CH ₃	C ₆ H ₁₁	71.7	150-151	3.21 (s)	6.98 (br)	3.83 (d)	0.9-2.4 (m)
2h	CH ₃	C ₆ H ₅	74.0	192-193	3.25 (s)	7.38 (br)	4.30 (d)	7.4-7.8 (m)

(a) Lit. (4) 135-136°. (b) Lit. (5) 200-202°. (c) Lit. (6,7) 228°.

Table 2

Analytical Data for Compounds **2a-h**

Compound No.	Formula	Calcd.			Found		
		C	H	N	C	H	N
2a	C ₃ H ₅ N ₃ O ₁	36.36	5.09	42.41	36.45	4.88	42.36
2b	C ₄ H ₇ N ₃ O ₁	42.47	6.27	37.15	42.33	6.41	37.18
2c	C ₆ H ₁₁ N ₃ O ₁	51.04	7.86	29.77	50.83	8.00	29.84
2d	C ₉ H ₁₅ N ₃ O ₁	59.64	8.34	23.19	59.46	8.31	23.03
2e	C ₉ H ₉ N ₃ O ₁	61.70	5.18	23.99	61.68	5.16	23.72
2f	C ₄ H ₇ N ₃ O ₁	42.47	6.24	37.15	42.46	6.24	37.29
2g	C ₁₀ H ₁₇ N ₃ O ₁	61.51	8.78	21.52	61.72	8.68	21.28
2h	C ₁₀ H ₁₁ N ₃ O ₁	63.47	5.86	22.21	63.23	5.85	22.22

semicarbazide with corresponding glyoxal or α -ketoacid derivatives according to the known methods (3).

Treatment of compound **1a** with an excess of sodium borohydride in refluxing methanol afforded compound **2a** exclusively, which was identical in every respect with an reported authentic sample (4). By the same method, compounds **2b-h** were synthesized in good yields from compounds **1b-h** (Equation 1) and their physical properties are consistent with the structures (Table 1,2). The pmr spectra of 2-methylated compounds **2f-h** ($R_1 = CH_3$) exhibited a broad signal about δ 9-10 due to 4-NH group, which was extinguished by addition of deuterium oxide, while another broad signal about δ 7 in compounds **2a-e** ($R_1 = H$) was assigned to 2-NH group. A methylene resonance was observed generally about δ 4 coupling with a neighboring 4-NH group. Therefore 4,5-dihydro structures are confirmed by the characteristic pmr spectra mentioned above.

The present reaction involves reductive demethylthiolation. A fast conversion was achieved under refluxing condition leading to suppression of by-products. Other reducing agents such as Raney-nickel, lithium aluminum hydride and zinc dust in aqueous acids were also examined, but their results were unsuccessful.

EXPERIMENTAL

The melting points are uncorrected. The pmr spectra were taken on a Varian XL-200 or Hitachi R-24B spectrometer in DMSO- d_6 using TMS as an internal standard.

General Procedure for Compound **2a-h**.

Compound **1** (3 mmoles) was dissolved in dry methanol (30 ml.) and sodium borohydride (12 mmoles) was added portionwise at room temperature. The solution was refluxed for 2 hours, then the solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel and eluted with chloroform-ethanol (15:1) in **2a-e** and hexane-acetone (3:1) in **2f-h** yielding pure product **2**. Physical data and yields are summarized in Table 1 and Table 2.

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