

A NOVEL ONE-STEP SYNTHESIS OF 3-SUBSTITUTED-5,6-DIHYDROTHIAZOLO[2,3-c]-1,2,4-TRIAZOLES AND -6,7-DIHYDRO-5H-1,2,4-TRIAZOLO[3,4-b][1,3]THIAZINES

L. G. Payne, M. T. Wu*, and A. A. Patchett

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc.

P. O. Box 2000, Rahway, New Jersey 07065, U.S.A.

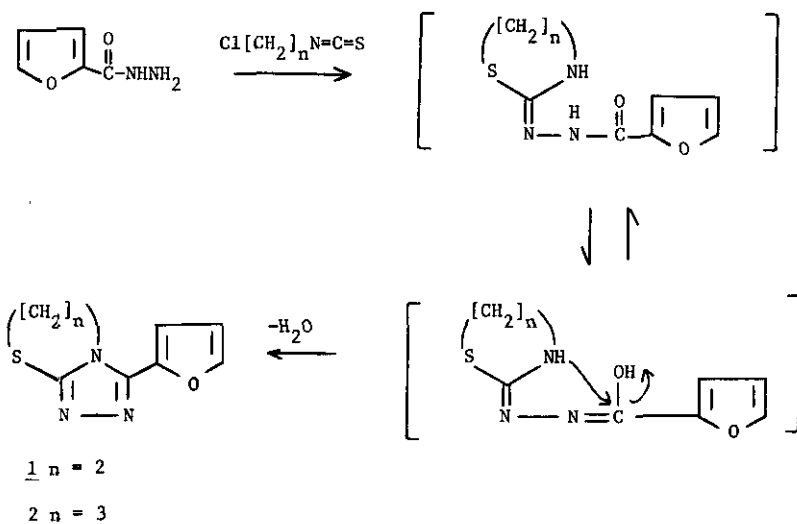
Abstract - 3-Substituted-5,6-dihydrothiazolo[2,3-c]-1,2,4-triazoles and -6,7-dihydro-5H-1,2,4-triazolo[3,4-b][1,3]-thiazines have been synthesized in one step by reaction of the acid hydrazides with haloalkyl isothiocyanates.

The availability and chemical versatility of haloalkyl isothiocyanates have made them useful starting materials for preparative heterocyclic chemistry. We have recently described a new one-step synthesis of 2,3-dihydro-5H-thiazolo[2,3-b]quinazolin-5-one and 3,4-dihydro-2H,6H-[1,3]-thiazino[2,3-b]quinazolin-6-one by the reaction of methyl anthranilate with chloroalkyl isothiocyanates.¹

In this communication we report the discovery of a novel general method for the synthesis of 3-substituted-5,6-dihydrothiazolo[2,3-c]-1,2,4-triazoles and -6,7-dihydro-5H-1,2,4-triazolo[3,4-b][1,3]thiazines.²

Reaction of 2-furoic acid hydrazide with 2-chloroethyl isothiocyanate³ in refluxing xylene followed by addition of triethylamine gave 3-(2-furanyl)-5,6-dihydrothiazolo[2,3-c]-1,2,4-triazole 1 in 59% yield as white leaflets, m.p. 142-143°C; ir ν_{\max} (Nujol): 1620 (C=N) and 1520 cm^{-1} (C=C); ¹Hnmr (CDCl₃): δ (ppm) 4.15 (t, 2H, CH₂S), 4.50 (t, 2H, CH₂N), 6.55 (q, H, FurH₄), 6.95 (d, 1H, FurH₃), 7.65 (s, 1H, FurH₅); ms (electron impact, 70 eV): m/e 193 (M⁺, base). The reaction involves the intermediate formation of a thiazoline and the elimination of water to give 1 via an intramolecular ring closure.



Similarly, we found that the reaction of 2-furoic acid hydrazide with 3-chloropropyl isothiocyanate and triethylamine,⁴ yielded 3-(2-furanyl)-6,7-dihydro-5H-1,2,4-triazolo[3,4-b][1,3]-thiazine 2 (80%), m.p. 211-212°C; ir ν_{\max} (Nujol): 1615 (C=N) and 1520 cm^{-1} (C=C); ¹Hnmr (DMSO-d₆): δ (ppm) 2.45 (m, 2H, C-CH₂-C), 3.30 (t, 2H, CH₂S), 4.43 (t, 2H, CH₂N), 6.63 (q, 1H, FurH₄), 7.25 (d, 1H, FurH₃), 7.90 (s, 1H, FurH₅); ms (electron impact, 70 eV): m/e 207 (M⁺, base).

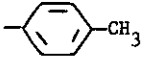


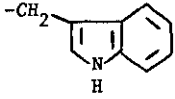


The physical and spectral properties of some representative examples are summarized in Table 1. The reaction is generally effective for a wide range of aliphatic, aromatic and heterocyclic acid hydrazides.

TABLE 1

Physical and Spectral Properties of Selected 3-Substituted-5,6-Dihydrothiazolo[2,3-c]-1,2,4-triazoles and -6,7-Dihydro-5H-1,2,4-triazolo[3,4-b][1,3]thiazines.

<u>R</u>	<u>n</u>	m.p. °C. (Solvent)	Yield, %	Spectral Data
	2	228.5-230 (Ethanol)	55	ir ν_{max} (Nujol): 1600, 1520 cm^{-1} ; $^1\text{Hnmr}$ (DMSO- d_6 + TFA): 4.15 (t, 2H, CH_2S), 4.70 (t, 2H, CH_2N), 7.80 (q, 4H, ArH); ms: m/e 237.
	2	192-193 (Ethanol)	42	ir ν_{max} (Nujol): 1640, 1585 cm^{-1} ; $^1\text{Hnmr}$ (DMSO- d_6): 4.15 (t, 2H, CH_2S), 4.55 (t, 2H, CH_2N), 7.52 (t, 1H, ArH), 8.20 (d, 1H, ArH), 8.70 (d, 1H, ArH), 9.00 (s, 1H, ArH); ms: m/e 204.

R	n	m.p. °C. (Solvent)	Yield, %	Spectral Data
	2	225.5-227 (Ethanol)	55	ir ν_{\max} (Nujol): 1630, 1615, 1540 cm^{-1} ; $^1\text{Hnmr}$ (DMSO- d_6): 2.45 (s, 3H, CH_3), 4.15 (t, 2H, CH_2S), 4.73 (t, 2H, CH_2N), 7.60 (q, 4H, ArH); ms: m/e 217.
- CH_3	3	154-156 (Xylene)	25	ir ν_{\max} (Nujol): 1530 cm^{-1} ; $^1\text{Hnmr}$ (CDCl_3): 2.2-2.6 (m, 2H, CCH_2C), 2.40 (s, 3H, CH_3), 3.20 (t, 2H, CH_2S), 4.00 (t, 2H, CH_2N); ms: m/e 155.
- $\text{CH}_2\text{CH}_2\text{CH}_3$	3	57-58 (EtOAc- Hexane)	67	ir ν_{\max} (Nujol): 1525 cm^{-1} ; $^1\text{Hnmr}$ (DMSO- d_6): 1.10 (t, 3H, $\text{CH}_2\text{CH}_2\text{CH}_3$), 1.75 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_3$); 2.40 (m, 2H, $-\text{SCH}_2\text{CH}_2\text{CH}_2\text{N}-$), 2.70 (t, 2H, $\text{CH}_2\text{CH}_2\text{CH}_3$), 3.25 (t, 2H, CH_2S), 4.05 (t, 2H, CH_2N), ms: m/e 183.
	3	186-187 (Ethanol)	62	ir ν_{\max} (Nujol): 1600, 1615, 1530 cm^{-1} ; $^1\text{Hnmr}$ (DMSO- d_6): 2.20 (m, 2H, $\text{C-CH}_2\text{-C}$), 3.23 (t, 2H, CH_2S), 4.15 (t, 2H, CH_2N), 7.70 (q, 4H, ArH); ms: m/e 251.
	3	163-164 (Ethanol)	63	ir ν_{\max} (Nujol): 1630, 1615, 1530 cm^{-1} ; $^1\text{Hnmr}$ (DMSO- d_6): 2.25 (m, CCH_2C), 2.45 (s, 3H, CH_3), 3.28 (t, 2H, CH_2S), 4.15 (t, 2H, CH_2N), 7.45 (q, 4H, ArH); ms: m/e 231.
	3	244-245 (Ethanol)	69	ir ν_{\max} (Nujol): 3150, 1620; 1530 cm^{-1} ; $^1\text{Hnmr}$ (DMSO- d_6): 2.20 (m, 2H, $-\text{SCH}_2-\text{CH}_2-\text{CH}_2\text{N}-$), 3.10 (t, 2H, CH_2S), 3.90 (t, 2H, CH_2N), 4.05 (s, 2H, CH_2S), 6.90 (s, 1H, C=CH), 7.20 (m, 4H, ArH), 7.50 (s, 1H, NH); ms: m/e 270.

ACKNOWLEDGEMENT

We wish to thank Mr. J. L. Smith for the mass spectra and Mr. J. P. Gilbert and his associates similarly for the microanalyses.

REFERENCES AND NOTES

Satisfactory analytical data have been obtained for all crystalline compounds described in this communication.

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Received, 14th June, 1979