(5) A. Bhati, *Chem. Commun.*, 476 (1965).
(6) Dimethyl ketal and *p*-toluenesulfonyl bromide in the mixtures were identified by comparison of their R_fs with those of authentic samples.
(7) W. A. F. Gladstone and R. O. C. Norman, *J. Chem. Soc. C*, 1532 (1966).
(8) Spectroscopic data are in agreement with those recorded on an authentic sample.
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Synthesis of *s*-Triazolo[3,4-*b*]benzothiazoles

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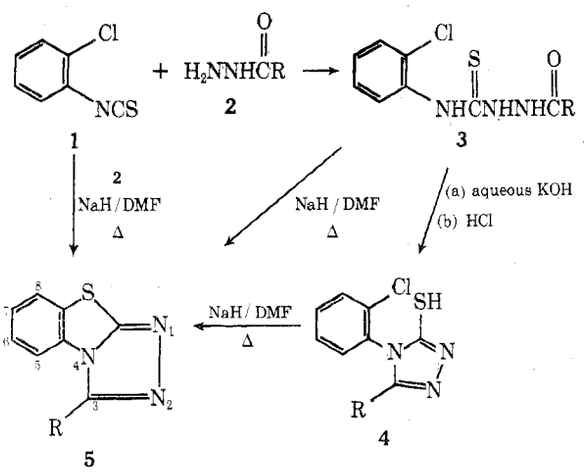
Received June 13, 1974

A general and convenient synthesis of *s*-triazolo[3,4-*b*]benzothiazoles is described. Treatment of 4-(2-halophenyl)-1-acyl-3-thiosemicarbazides with sodium hydride and heating to reflux in dimethylformamide yielded *s*-triazolo[3,4-*b*]benzothiazoles.

Syntheses of *s*-triazolo[3,4-*b*]benzothiazoles have been reported by Reynolds and Van Allan[1] as well as Butler, O'Sullivan and Scott.[2,3] Reynolds and Van Allan reported various cyclodehydration reactions of the 2-benzothiazoylhydrazides, while Butler, *et al.*, reported the oxidative cyclizations of the substituted benzothiazolylhydrazones. In all instances, an extended synthetic sequence is necessary to obtain various *s*-triazolo[3,4-*b*]benzothiazoles. We would like to report a novel ring-forming reaction for the synthesis of *s*-triazolo[3,4-*b*]benzothiazoles. The method allows a variety of substituted *s*-triazolo[3,4-*b*]benzothiazoles to be obtained in a series of facile reactions. This method is outlined in Scheme I.

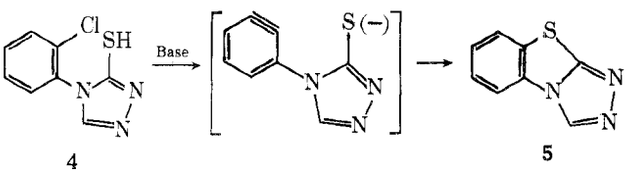
Scheme I



Compounds **3** and **4** (R = H) were readily synthesized in the manner outlined. Heating the potassium salt of **4** in refluxing dimethylformamide (DMF)[4] yielded the *s*-triazolo[3,4-*b*]benzothiazole (**5**, R = H). This compound was identical with a sample prepared by the method of Reynolds and Van Allan[1] from the reaction of 2-hydrazinobenzothiazole with triethyl orthoformate. However, simply treating compounds **4** or **3** with sodium hydride followed by heating to reflux in DMF gave compound **5** in similar yields. Thus, it is now possible to prepare *s*-triazolo[3,4-*b*]benzothiazole (**5**) in only two steps. Compound **1** can also be directly converted to compound **5** but the product from this method is difficult to purify.

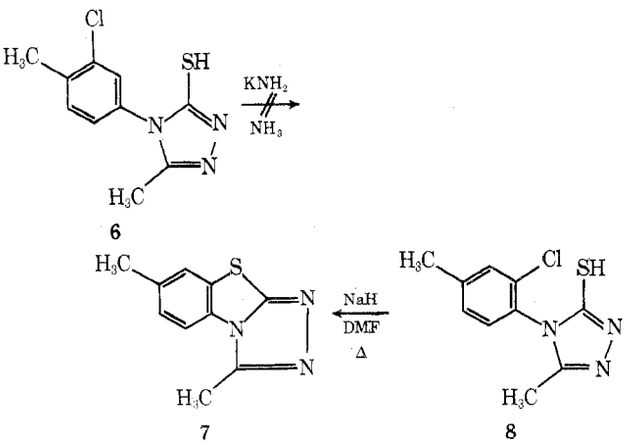
Utilization of appropriately substituted acylhydrazides (**2**) in this reaction ultimately results in substitution at the 3 position of compound **5**. Substituents may also be placed in the 5, 6, or 7 positions of compound **5** through the utilization of the appropriately substituted 2-halophenyl isothiocyanate (**1**) in this reaction. Tables I and II illustrate some of the possible variations.

A possible mechanism for the formation of *s*-triazolo[3,4-*b*]benzothiazoles from the triazole-3-thiols would be a nucleophilic displacement by the thiolate anion. Alternatively, the mechanism could involve elimination of a halogen to yield a benzyne followed by thiolate addition to close the ring.



Ogura and Itoh[5] reported the synthesis of imidazo[2,1-*b*]benzothiazoles *via* a benzyne intermediate from 1-(3-chlorophenyl)-2-mercaptoimidazole and liquid ammonia potassium amide.

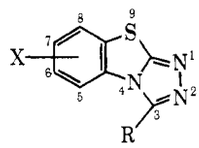
In this instance a benzyne mechanism is not probable since 4-(3-chloro-4-methylphenyl)-5-methyl-1,2,4-triazole-3-thiol (**6**) did not yield 3,7-dimethyl-*s*-triazolo[3,4-*b*]benzothiazole (**7**) under their reaction conditions or under the conditions employed in the synthesis of compound **7** from compound **8**.



Experimental Section

All chemicals were reagent grade and used without further purification. The products separated were characterized by elemental analysis, nmr, and mass spectra. All isothiocyanates were commercial grade or prepared from the aniline according to the literature. All melting points were uncorrected and were determined in a capillary tube using a Mel-Temp apparatus. The acylhydrazines were of commercial quality or were prepared by standard methods.

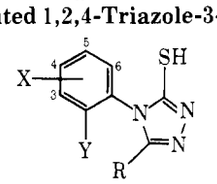
Table I
Substituted *s*-Triazolo[3,4-*b*]benzothiazoles



Compd no.	X	R	Mp, °C	% Yield	Analyses (Calcd/Found) C	H	N
5	H	H	175–176 (lit.[1] mp 178)	10,[a] 30,[b-d] 70[e]	54.84/54.56	2.88/2.94	23.98/23.79
7	7-CH_3	CH_3	176–177	45[c]	59.09/58.21	4.46/4.59	20.67/19.66
11	5-Cl	CH_3	186–188	55[c]	46.69/46.98	2.35/2.56	16.34/16.07
13	H	CH_3	153–154 (lit.[1] mp 156)	20,[b] 30[c]	57.12/56.84	3.73/3.79	22.21/22.23
15	6-CF_3	CH_3	181–183	30[c]	48.33/48.62	2.70/2.95	18.79/18.96
17	6-CH_3	CH_3	203–207	50[c]	59.09/58.80	4.46/4.43	20.67/20.42
19	6-Cl	CH_3	264–266	10[c]	48.33/48.27	2.70/2.75	18.79/18.97
21	7-Cl	CH_3	186–188	45[c]	48.33/48.32	2.70/2.89	18.79/18.96
23	H	C_7H_{15}	82–84	45[c]	65.90/66.01	7.01/6.91	15.37/15.27

[a] Method A. [b] Method B. [c] Method C. [d] Method C *via* fluoro displacement. [e] Method D.

Table II
Substituted 1,2,4-Triazole-3-thiols



Compd no.	X	R	Y	Mp, °C	Analyses (Calcd/Found) C	H	N
4	H	H	Cl	195–196	45.39/45.48	2.86/3.10	19.85/19.70
6	3-Cl, 4-CH_3	CH_3	H	237–240	50.10/49.87	4.20/3.99	17.53/17.26
8	4-CH_3	CH_3	Cl	243–244	50.10/50.23	4.20/4.24	17.53/17.73
9	H	H	F	166–167	49.22/49.09	3.10/3.13	21.53/21.37
10	6-Cl	CH_3	Cl	240–242	41.55/41.32	2.71/2.80	16.15/15.98
12	H	CH_3	Cl	217–219	47.89/47.73	3.57/3.64	18.62/18.39
14	5-CF_3	CH_3	Cl	208–209	40.90/40.95	2.40/2.42	14.31/14.27
16	5-CH_3	CH_3	Cl	229–231	50.10/49.89	4.20/4.27	17.53/17.40
18	5-Cl	CH_3	Cl	248–250	41.55/41.85	2.71/3.00	16.15/16.40
20	4-Cl	CH_3	Cl	248–253	41.55/41.57	2.71/2.81	16.15/16.37
22	H	C_7H_{15}	Cl	150–157	58.14/57.95	6.51/6.33	13.56/13.79

Preparation of Acylated Thiosemicarbazides. All the thiosemicarbazides were prepared from the phenyl isothiocyanate and the acylhydrazines. The following specific preparations are exemplary of the methods and may be considered general.

A. Preparation of 4-(2-Chlorophenyl)-1-formyl-3-thiosemicarbazide (3). A solution of 50.6 g (0.33 mol) of 2-chlorophenyl isothiocyanate and 20 g (0.33 mol) of formylhydrazine in 500 ml of tetrahydrofuran was heated to reflux for 7 hr. The reaction mixture was allowed to cool and the insoluble product was collected by filtration and washed with water. The yield was 68 g (98%) of 4-(2-chlorophenyl)-1-formyl-3-thiosemicarbazide, mp 172–173°. *Anal.* Calcd for $C_8H_8ClN_3OS$: C, 41.83; H, 3.51; N, 18.29. Found: C, 41.61; H, 3.55; N, 18.14.

B. Preparation of 1-Acetyl-4-(2-chloro-5-methylphenyl)-3-thiosemicarbazide. A solution of 18.3 g (0.10 mol) of 2-chloro-5-methylphenyl isothiocyanate and 11.0 g (0.15 mol) of acethydrazine in 500 ml tetrahydrofuran was heated to reflux for 7 hr. After cooling, the insoluble product was collected by filtration and washed with water. The yield was 25 g (97%) of 1-acetyl-4-(2-chloro-5-methylphenyl)-3-thiosemicarbazide, mp 145–147°. *Anal.* Calcd for $C_{16}H_{12}ClN_3O_2S$: C, 46.60; H, 4.69; N, 16.30. Found: C, 46.87; H, 4.92; N, 16.58.

Preparation of the 1,2,4-Triazole-3-thiols. The following specific preparation is exemplary of the method and may be considered general.

Preparation of 4-(2-Fluorophenyl)-1,2,4-triazole-3-thiol (9). A solution of 1.1 g (0.020 mol) of potassium hydroxide in 50 ml of water was stirred while 3.5 g (0.016 mol) of 4-(2-fluorophenyl)-1-formyl-3-thiosemicarbazide was added. The solution was warmed on a steam bath for 1 hr. After cooling, the solution was poured into a dilute hydrochloric acid solution. The insoluble product was collected by filtration and washed with water. The yield was 2.5 g (81%) of 4-(2-fluorophenyl)-1,2,4-triazole-3-thiol, mp 166–167°. *Anal.* Calcd for $C_8H_6FN_3S$: C, 49.22; H, 3.10; N, 21.53. Found: C, 49.09; H, 3.13; N, 21.37.

Preparation of *s*-Triazolo[3,4-*b*]benzothiazoles. The following specific preparations are exemplary of the methods and may be considered general.

Method A. A solution of 1.8 g (0.030 mol) of formylhydrazine in 50 ml of dry dimethylformamide (DMF) was added to a stirred solution of 5 g (0.030 mol) of 2-chlorophenyl isothiocyanate in 50 ml of dry DMF. The solution was then heated to 60° for 24 hr. After cooling, 1.5 g (0.030 mol) of sodium hydride as a 50% mineral oil dispersion was added and the mixture heated at reflux to complete the reaction. After cooling, the solution was poured into water and filtered. The aqueous solution was washed with hexane and the product was extracted with ethyl acetate to yield *s*-triazolo[3,4-*b*]benzothiazole (5), mp 175–176°. *Anal.* Calcd for $C_8H_5N_3S$: C, 54.85; H, 2.88; N, 23.98. Found: C, 54.56; H, 2.94; N, 23.79.

Method B. A solution of 2.4 g (0.010 mol) of 1-acetyl-4-(2-chlo-

rophenyl)-3-thiosemicarbazide in 50 ml of dry DMF was treated with 0.5 g (0.010 mol) of sodium hydride as a 50% mineral oil dispersion. After heating to reflux for 126 hr, the solution was poured into water and washed with hexane. The product was extracted with ethyl acetate to yield 3-methyl-*s*-triazolo[3,4-*b*]benzothiazole (**13**), mp 152–154°. *Anal.* Calcd for $C_9H_7N_3S$: C, 57.12; H, 3.73; N, 22.21. Found: C, 56.84; H, 3.79; N, 22.23.

Method C. A solution of 5 g (0.019 mol) of 4-(2,4-dichlorophenyl)-5-methyl-1,2,4-triazole-3-thiol (**20**) in 100 ml of dry DMF was treated with 1 g (0.020 mol) of sodium hydride as a 50% mineral oil dispersion. The solution was heated to reflux for 24 hr and, after cooling, poured into water. The aqueous solution was washed with hexane and the product was extracted with ethyl acetate to yield 7-chloro-3-methyl-*s*-triazolo[3,4-*b*]benzothiazole (**21**), mp 186–188°. *Anal.* Calcd for $C_9H_6ClN_3S$: C, 48.33; H, 2.70; N, 18.79. Found: C, 48.32; H, 2.89; N, 18.96.

Method D. A solution of 2.0 g (0.0083 mol) of potassium 4-(2-chlorophenyl)-1,2,4-triazole-3-thiolate in 100 ml of dry DMF was heated to reflux for 24 hr. The solution was concentrated to a residue in *in vacuo* and washed with hexane. The resulting solid was extracted with ethyl acetate. The ethyl acetate solution yielded 1 g of *s*-triazolo[3,4-*b*]benzothiazole (**5**), mp 174–176°. *Anal.* Calcd for $C_8H_5N_3S$: C, 54.84; H, 2.88; N, 23.98. Found: C, 53.83; H, 2.90; N, 23.33.

Registry No.—**1,** 2740-81-0; **2** (R = H), 624-84-0; **2** (R = CH_3), 1068-57-1; **3** (R = H), 52747-49-6; **3** (R = CH_3), 52747-50-9; **3** (R = C_7H_{15}), 52747-51-0; **4** (R = H), 52747-52-1; **5** (R = H), 247-92-7; **6,** 52747-53-2; **7,** 52747-54-3; **8,** 52747-55-4; **9,** 52747-56-5; **10,** 52747-57-6; **11,** 52747-58-7; **12,** 52747-59-8; **13,** 41814-60-2; **14,** 52747-60-1; **15,** 52747-61-2; **16,** 52747-62-3; **17,** 52747-63-4; **18,** 52747-64-5; **19,** 52747-65-6; **20,** 52747-66-7; **21,** 52747-67-8; **22,** 52747-68-9; **23,** 52747-69-0; 1-acetyl-4-(2-chloro-5-methylphenyl)-3-thiosemicarbazide, 52768-72-6; 2-chloro-5-methylphenyl isothiocyanate, 52747-70-3; 4-(2-fluorophenyl)-1-formyl-3-thiosemicarbazide, 52747-71-4; potassium 4-(2-chlorophenyl)-1,2,4-triazole-3-thiolate, 52747-72-5; 1-acetyl-4-(3-chloro-4-methylphenyl)-3-thiosemicarbazide, 52747-76-9; 1-acetyl-4-(2-chloro-4-methylphenyl)-3-thiosemicarbazide, 52747-73-6; 1-acetyl-4-(2,6-dichlorophenyl)-3-thiosemicarbazide, 52747-77-0; 1-acetyl-4-(2-chloro-5-trifluoromethylphenyl)-3-thiosemicarbazide, 52747-74-7; 1-acetyl-4-(2,5-dichlorophenyl)-3-thiosemicarbazide, 52747-75-8; 1-acetyl-4-(2,4-dichlorophenyl)-3-thiosemicarbazide, 52795-85-4.

References and Notes

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(2) R. N. Butler, P. O'Sullivan, and F. L. Scott, *J. Chem. Soc. C,* 2265 (1971); *Chem. Abstr.*, **75,** 48963.
(3) R. N. Butler, P. O'Sullivan, and F. L. Scott, *J. Chem. Soc., Perkin Trans. 1,* 1519 (1972); *Chem. Abstr.*, **77,** 61867.
(4) Other higher boiling amide solvents such as *N,N*-dibutylacetamide, *N,N*-dimethylacetamide, and *N*-methyl-2-pyrrolidone can also be used in this reaction.
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Studies on the Isomerization of 4-(1-Aziridinyl)quinazolines to 2,3-Dihydroimidazo[1,2-*c*]quinazolines

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Received April 17, 1974

The iodide ion catalyzed isomerization of several 4-(1-aziridinyl)quinazolines to 2,3-dihydroimidazo[1,2-*c*]quinazolines has been investigated in relation to the stereochemical outcome of the reaction. The rearrangement of cis- and trans-2,3-disubstituted aziridines is quite stereoselective; the selectivity is greater when the aziridine ring is disubstituted with methyl rather than phenyl groups. In any case the stereoselectivity of the isomerization varies with the iodide ion concentration. Oxidation of 2,3-dihydroimidazo[1,2-*c*]quinazolines with chloranil yields good amounts of imidazo[1,2-*c*]quinazoline and its derivatives.

The imidazo[1,2-*c*]quinazoline ring system (**1**) has been little explored and only a few derivatives are described in the chemical literature.[1-6] Two of us have recently reported a synthesis of **1** based on the manganese dioxide oxidation of the 5,6-dihydroimidazo[1,2-*c*]quinazoline (**2**) obtained in low yield by treatment of 2-(*o*-nitrophenyl)-1-hydroxyimidazole 3-oxide with zinc powder and formic acid.[7]

This paper describes a novel three-step synthetic route to **1** by chloranil oxidation of 2,3-dihydroimidazo[1,2-*c*]quinazoline (**4**), which is easily prepared by iodide ion catalyzed isomerization of 4-(1-aziridinyl)quinazoline (**3**) (Scheme I).

Through the isomerization of suitable aziridines, a wide variety of five-membered heterocyclic ring compounds is obtained.[8] While the rearrangement of *N*-acylaziridines to the isomeric 2-aryl- or 2-alkyl-Δ^2-oxazoline ring system by some nucleophilic ions has been the subject of a number of studies,[8a,9] the opposite is true for the nucleophile-catalyzed isomerization of aziridine derivatives such as **5,** which, probably through the intermediate ambident anion

Scheme I