# Bridgehead Nitrogen Heterocycles. II. Formation by Reaction of α-Amino N-Heterocyclic Compounds with Chlorothioformyl Chloride

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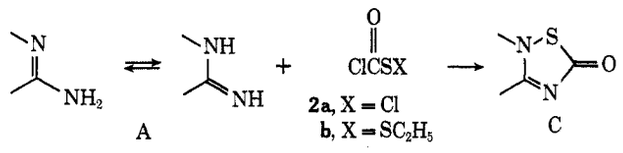
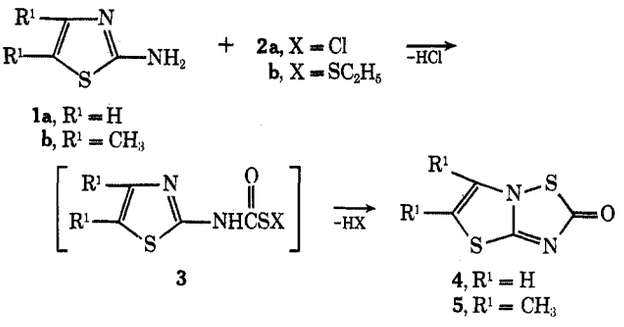
Cyclization of a variety of α-amino N-heterocyclic compounds (A) with chlorothioformyl chloride (**2a**) resulted in the formation of bicyclic bridgehead nitrogen heterocycles (C) in fair yield. A second method of synthesis of C, from A and ethyldithiocarbonyl chloride (**2b**), has also been established. Some preliminary studies of the chemical reactivity of 6-substituted 2*H*-[1,2,4]thiadiazolo[2,3-*b*]pyridazin-2-ones (**14**) and **15** have been carried out.

The preparation of bridgehead nitrogen heterocycles from α-amino N-heterocyclic compounds with 3-chloroacrylic and atropic acids (and acid chlorides) was investigated recently in this laboratory.[1] We have now investigated the reactions of α-amino N-heterocyclic compounds with chlorothioformyl chloride (**2a**) which build up novel nitrogen- and sulfur-containing heterocyclic ring systems with bridgehead nitrogen.



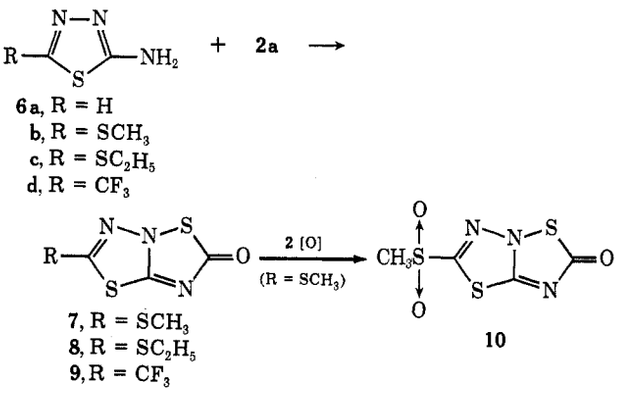

## Results

Entry into the 2*H*-thiazolo[3,2-*b*][1,2,4]thiadiazol-2-one ring system was first obtained when 2-aminothiazole (**1a**) and its 4,5-dimethyl analog (**1b**) were allowed to react with **2a** in the presence of 2 molar equiv of triethylamine in tetrahydrofuran solution at temperatures between −10 and 60°. The reaction mixtures from these two amines were black tars, but it was possible to isolate and characterize **4** and **5**. The yields of **4** and **5**

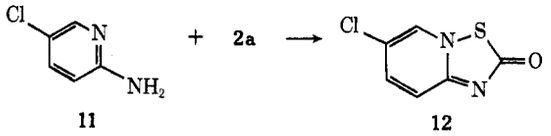



were in the order of 2–3%. This appears to be more of an unsatisfactory reaction than an isolation problem, as **5** was purified and readily isolated by silica chromatography.[2] Because of the inherent synthesis difficulty, an alternative route was sought. A suitable intermediate would be ethyldithiocarbonyl chloride (**2b**) which would be expected to undergo amination by the heterocyclic amine followed by a facile ring closure to the bicyclic ring system. It was found that **1a** reacted readily with **2b** and the yield of purified **4** was in the order of 25% without isolation of the intermediate **3** ($R^1$ = H; X = $SC_2H_5$). The formation of **3** ($R^1$ = H; X = $SC_2H_5$) in admixture with **4** at 0° was likely in light of tlc data (Experimental Section). However, attempted isolation of **3** at room temperature proved unsuccessful.

The 1,3,4-thiadiazole ring system has been the subject of numerous investigations.[4] It was anticipated that the most direct route to the 6*H*-[1,3,4]thiadiazolo-[3,2-*b*][1,2,4]thiadiazol-6-one system would be from 2-amino-1,3,4-thiadiazole (**6a**) and its 5-substituted analogs (**6b**, **6c**, and **6d**). Reaction of **6a** with **2a** led to the formation of tar which could not be resolved by chromatography. However, condensations of **6b**, **6c**, and **6d** with **2a** occurred readily, under the same reaction conditions used for the reactions of **2a** with **1**, to give the fused heterocyclic compounds **7**, **8**, and **9** in 10–53% yield. Oxidation of **7** with *m*-chloroperbenzoic acid gave the corresponding sulfone **10**.




Entry into the 2*H*-[1,2,4]thiadiazolo[2,3-*a*]pyridin-2-one system was obtained when **2a** was allowed to react with 2-amino-5-chloropyridine (**11**). Recrystallization of the reaction mixture afforded **12** in 48% yield.




2-Amino-6-chloropyridazine (**13**) also underwent ready reaction with **2a** to yield 6-chloro-2*H*-[1,2,4]-thiadiazolo[2,3-*b*]pyridazin-2-one (**14**) in 37% yield. The displacement of chlorine in **14** was quite facile, and reaction at ambient temperature of sodium methylmercaptide with **14** led to the 6-methylthio analog (**15**). Oxidation of **15** with peracetic acid gave the sulfone **16**,

(1) J. G. Kuderna, R. D. Skiles, and K. Pilgram, *J. Org. Chem.*, **36**, 3506 (1971).

(2) A possible explanation for the low yields may be the inherent instability of **3** ($R^1$ = H, $CH_3$; X = Cl). For example, *N*,*N*-dialkylcarbamoylsulfenyl chlorides readily decompose at 0° with elimination of sulfur to form *N*,*N*-dialkylcarbamoyl chlorides.[3]

(3) G. Zumach and E. Kühle, *Angew. Chem.*, **82**, 63 (1970); *Angew. Chem., Int. Ed. Engl.*, **9**, 54 (1970).

(4) L. L. Bambas, *Heterocycl. Compounds*, **4**, 81 (1952).

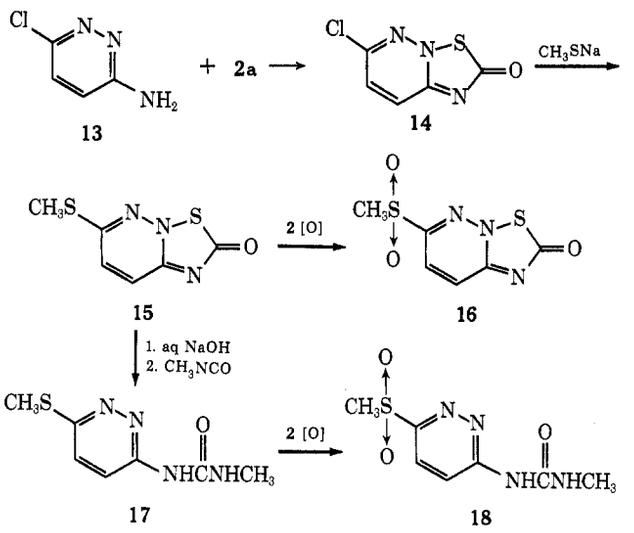
TABLE I
HETEROCYCLES OBTAINED BY REACTION OF α-AMINO N-HETEROCYCLIC COMPOUNDS WITH CHLOROTHIOFORMYL CHLORIDE (CTFC)[a]

| Compd | Yield, % | Mp, °C | Formula | Nmr data, δ[b] | Solvent |
|---|---|---|---|---|---|
| **4** | 3.3<br>25[c] | 130–132 | $C_4H_2N_2OS_2$ | 7.6 (1) (d, 1, 5-CH), 7.2 (1) (d, 6-CH) | DMSO-$d_6$ |
| **5** | 2.0 | 73–75 | $C_6H_6N_2OS_2$ | 2.1 (1) (d, 3, 5-$CH_3$), 2.4 (1) (d, 3, 6-$CH_3$) | $CDCl_3$ |
| **7** | 10 | 149–152 | $C_4H_3N_3OS_3$ | 2.75 (s, $SCH_3$) | $CDCl_3$ |
| **8** | 36.4 | 104–106 | $C_5H_5N_3OS_3$ | 1.5 (t, 3, $CH_3$), 3.35 (q, 2, $CH_2$) | $CDCl_3$ |
| **9** | 53 | 83–85 | $C_4F_3N_3OS_2$ | | |
| **12** | 48 | 132–134 | $C_6H_3ClN_2OS$ | 7.4 (m, 2, CH=CH), 8.1 (m, 1, 5-CH) | DMSO-$d_6$ |
| **14** | 37 | 164–166 | $C_5H_2ClN_3OS$ | 7.45 (q, 1, CH=), 7.9 (q, 1, CH=) | DMSO-$d_6$ |
| **20** | 20 | 77–79 | $C_5H_6N_2OS_2$ | 1.4 (m, 2, 6-$CH_2$), 3.1 (t, 2, 5-$CH_2$), 3.85 (t, 2, 7-$CH_2$) | $CDCl_3$ |

[a] Satisfactory analytical data (±0.3 for N) were reported for all compounds in this table; C and H analyses were reported for all except **7**; S analyses were reported for **4**, **7**, **8**, and **20**; Cl analysis was reported for **14**. [b] In parts per million (*J* in hertz) (multiplicity, number of protons, assignment). [c] From 2-aminothiazole and ethyldithiocarbonyl chloride.

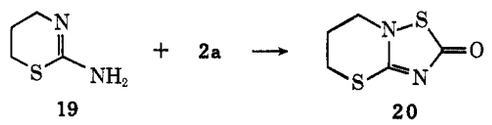
whereas alkaline hydrolysis afforded 3-amino-6-methylthiopyridazine isolated as its urea **17** by reaction with methyl isocyanate; oxidation of **17** gave sulfone **18** (Scheme I) in 90% yield. Displacement of chlorine

SCHEME I




in **14** by nucleophiles other than sodium methylmercaptide followed by hydrolysis of the resulting substituted bicyclic heterocycle may provide a convenient preparative method for 3-substituted 6-aminopyridazines which are difficult to prepare by other methods.[5,6]

5,6-Dihydro-2-amino-4*H*-1,3-thiazine (**19**) underwent ready reaction with **2a** to yield 5,6-dihydro-2*H*-[1,2,4]-thiadiazolo[3,2-*b*]thiazin-2-one (**20**), also a new heterocyclic system.

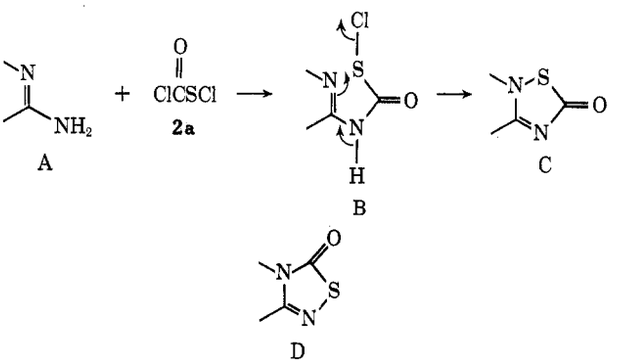



## Discussion

Analytical and physical data of all bicyclic heterocycles prepared by reaction of an α-amino N-heterocyclic compound, **1**, with **2a** are summarized in Table I. A common feature of the mass spectra of the compounds described above is that the molecular ions are prominent peaks indicating a fairly great stability of these fused bicyclic compounds. The primary fragmentation path involves loss of the carbonyl group. In all cases, ions corresponding to $M^+ - 28$ (CO) can be observed which on further impact lose nitrogen and sulfur. However, certain substituents (*e.g.*, $CF_3$, RS, and $RSO_2$) influence the secondary pattern markedly.

In the ir spectra, carbonyl bands for all the bicyclic heterocycles are near 1700 $cm^{-1}$, whereas absorptions of the -C=N grouping are shown by all compounds in the 1640–1670-$cm^{-1}$ region.

The chemistry of α-amino N-heterocyclic compounds (amidines) of general structure A is complicated by the presence in the molecule of two nitrogen atoms, and it is frequently difficult to present unequivocal chemical proof of structure of reaction products. The problem is still more complicated by the presence of two reactive centers in **2a**. Basically, the reaction of A with **2a** may give either one of the two heterocycles C and D. Structure D may be excluded from consideration on the basis of the following grounds. Firstly, in α-amino N-heterocyclic compounds of general structure A, monoacylation and carbamoylation occurs always on the exocyclic amino group.[5,7–11] Secondly, **2a** has been shown[8] to undergo reaction with amines selectively with the carbonyl group forming an amide bond leaving B as the only likely intermediate. Soft–hard acid–base theory[12,13] supports this view in that amidines such as A (the amino group is a hard base) would be expected




(5) M. Tisler and B. Stanovnik, *Advan. Heterocycl. Chem.*, **9**, 211 (1968).
(6) J. Druey, K. Meier, and K. Eichenberger, *Helv. Chim. Acta*, **37**, 121 (1954).
(7) A. Schöberl and K. H. Magosch, *Justus Liebigs Ann. Chem.*, **742**, 74 (1971).
(8) F. Kröhnke, B. Kickhöfer, and C. Thoma, *Ber.*, **88**, 1117 (1955).
(9) F. Kurzer, *Advan. Heterocycl. Chem.*, **5**, 168 (1965).
(10) J. Sandström, *ibid.*, **9**, 181 (1968).
(11) A. H. Land, *Heterocycl. Compounds*, **5**, 595 (1957).
(12) R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3553 (1963).
(13) We are grateful to reviewer III who raised this point.

to react preferentially with the carbonyol group (carbonyl carbon centers which resemble carbonium centers are hard) of **2a**. The internal nitrogen atom in B would be expected to react more slowly with the sulfur atom (a soft acid) to give C.

In summary, synthetic procedures were developed to convert $\alpha$-amino N-heterocyclic compounds to a variety of novel bridgehead nitrogen heterocycles by reaction with chlorothioformyl chloride. Detailed studies of the individual synthesis to optimize conditions were not performed.

## Experimental Section

Melting points are uncorrected and were taken on a Thomas-Hoover capillary apparatus. Ir absorption spectra were determined on a Beckman IR-4 double beam instrument. The nmr spectra were determined on a Varian A-60 spectrometer. Mass spectra were recorded on a Perkin-Elmer Model 270 B double focusing mass spectrometer.

**Materials.**—2-Aminothiazole (**1a**) and 2-amino-5-chloropyridine (**11**) (Aldrich Chemical Co.) were used without further purification. The following $\alpha$-amino N-heterocyclic compounds were prepared following procedures reported in the literature: 2-amino-1,3,4-thiadiazole (**6a**),[14] 2-amino-5-methylthio-1,3,4-thiadiazole (**6b**),[15] 3-amino-6-chloropyridazine (**13**),[16] 2-amino-5-trifluoromethyl-1,3,4-thiadiazole (**6d**),[17] 2-amino-4,5-dimethylthiazole (**1b**),[18] and 5,6-dihydro-2-amino-4*H*-1,3-thiazine (**19**).[8]

**2-Amino-5-ethylthio-1,3,4-thiadiazole (6c).**—Alkylation with ethyl iodide of the sodium salt of 2-amino-5-mercapto-1,3,4-thiadiazole proceeded smoothly in refluxing ethanol to give the title compound in 88% yield, mp 134–136°.

*Anal.* Calcd for $C_4H_7N_3S_2$: C, 41.4; H, 5.7; N, 16.1; S, 36.8. Found: C, 41.6; H, 6.0; N, 16.0; S, 36.5.

**2*H*-Thiazolo[3,2-*b*][1,2,4]thiadiazol-2-one (4). A. From 2-Aminothiazole (1a) and Chlorothioformyl Chloride (2a).**—To a cold (−10°) solution of 13.1 g (0.1 mol) of **2a** in 100 ml of tetrahydrofuran was added dropwise (75 min) with stirring a solution of 10.0 g (0.1 mol) of **1a** in 300 ml of tetrahydrofuran, followed by the dropwise (30 min) addition of 20.2 g (0.2 mol) of triethylamine. The mixture was then stirred at 60° for 2.5 hr and filtered. The filtrate was concentrated to dryness and the residual solid was recrystallized from methanol to afford 0.5 g (3.3%) of **4**: a brown crystalline solid; mp 130–132°; ir (KBr) 1735, 1645 cm$^{-1}$; mass spectrum (70 eV) 158 (M$^+$).

**B. From 2-Aminothiazole (1a) and Ethyldithiocarbonyl Chloride (2b).**—To a cooled (0°) solution of 14.4 g (0.1 mol) of **2b** in 100 ml of tetrahydrofuran was added dropwise with stirring a solution of 20.0 g (0.2 mol) of **1a** in 150 ml of tetrahydrofuran causing a tarry solid to precipitate. Tlc of the solution indicated the disappearance of starting materials and the appearance of two new reaction products. The intensity of the spot corresponding to the compound with smaller $R_f$ value, presumably **3** ($R^1$ = H; X = $SC_2H_5$), decreased with time at the expense of the spot corresponding to **4** which has a greater $R_f$ value. The mixture was stirred for 18 hr at ambient temperature, heated to 60° for 1 hr, and cooled to 25°. Filtration and concentration to dryness of the filtrate afforded a solid which was recrystallized from methanol to give 4.0 g (25%) of **4**, a light yellow crystalline solid, mp 130–132°, in admixture with A (see above), mmp 130–132°. $R_f$ values of **3** ($R^1$ = H; X = $SC_2H_5$) (solvent no.): 0.09 (3),[19] 0.17 (9),[19] and 0.36 (10).[19] $R_f$ values of **4** (solvent no.): 0.37 (3), 0.44 (9), and 0.56 (10).

**5,6-Dimethyl-2*H*-thiazolo[3,2-*b*][1,2,4]thiadiazol-2-one (5).**—To a solution of 7.2 g (0.05 mol) of **2a** in 100 ml of tetrahydrofuran was added at 5° dropwise and with stirring a solution of 7.0 g (0.055 mol) of **1b**. The temperature was maintained at 5° during the dropwise (1.5 hr) addition of 11.0 g (0.109 mol) of triethylamine. The mixture was stirred at ambient temperature for 1 hr and then heated to 60° for 1 hr. The warm reaction mixture was filtered and the filtrate was evaporated to a residue which upon purification by column chromatography afforded 0.2 g (2%) of **5**: mp 73–75°; ir (KBr) 1705 (C=O), 1670 cm$^{-1}$ (C=); mass spectrum (70 eV) 186 (M$^+$).

**2-Methylthio-6*H*-[1,3,4]thiadiazolo[3,2-*b*][1,2,4]thiadiazol-6-one (7).**—To a solution of 13.1 g (0.1 mol) of **2a** in 150 ml of tetrahydrofuran was added at −5° with stirring a solution of 14.7 g (0.1 mol) of **6b** and 20.2 g (0.2 mol) of triethylamine in 350 ml of tetrahydrofuran. The mixture was warmed gently to reflux for 2.5 hr. The reaction mixture was filtered, concentrated to dryness, and purified by column chromatography over silica gel to give 2.0 g (10%) of **7**, a light yellow crystalline solid, mp 149–152°.

**2-Methylsulfonyl-6*H*-[1,3,4]thiadiazolo[3,2-*b*][1,2,4]thiadiazol-6-one (10).**—To a solution of 2.0 g (0.01 mol) of **7** in 25 ml of chloroform was added with stirring a solution of 6.1 g (0.03 mol) of 85% *m*-chloroperbenzoic acid in 25 ml of chloroform. The mixture was stirred at ambient temperature for 2.5 hr and left standing overnight. The reaction mixture was washed with aqueous (10%) sodium carbonate and then with cold water. The chloroform layer was dried and evaporated to dryness. The residual solid was recrystallized from methanol to give 0.5 g (22%) of **10**: a light yellow colored solid; mp 145–148°; ir (KBr) 1742, 1728, 1708, (C=O), 1560 (C=), 1160 cm$^{-1}$ ($SO_2$); mass spectrum (70 eV) 237 (M$^+$), 221, 209, 123, 107, 102, 90, 79, 63, 44, 28, 15.

*Anal.* Calcd for $C_4H_3N_3O_3S_3$: C, 20.2; H, 1.3; N, 17.7. Found: C, 20.4; H, 1.4; N, 17.8.

**6-Chloro-2*H*-[1,2,4]thiadiazolo[2,3-*b*]pyridazin-2-one (14).**—To a chilled (5°) solution of 13.1 g (0.1 mol) of **2a** in 100 ml of tetrahydrofuran was added dropwise (2.5 hr) with stirring a solution of 12.9 g (0.1 mol) of **13** and 20.2 g (0.2 mol) of triethylamine in 600 ml of tetrahydrofuran. The mixture was heated to reflux for 6 hr, filtered while hot, and concentrated to dryness. The residual solid was recrystallized from methanol (charcoal) to give 7.0 g (37%) of **14**: a light yellow crystalline solid; mp 164–167°; ir (KBr) 1720 (C=O), 1660, 1620 cm$^{-1}$ (C=).

**6-Methylsulfonyl-2*H*-[1,2,4]thiadiazolo[2,3-*b*]pyridazin-2-one (16).**—A solution of 4.0 g (21.4 mmol) of **14** and 1.5 g (21.4 mmol) of sodium methylmercaptide in 40 ml of dimethyl sulfoxide was left standing at ambient temperature for 1.5 hr. A solid precipitated during this time. The mixture was poured over ice and filtered. The filter cake was washed with water and dried to give 3.0 g (72%) of **15**.

Compound **15**, 1.5 g, was suspended in 25 ml of acetic acid and warmed to 50° until solution occurred. Hydrogen peroxide (35%, 10 ml) was added. The mixture was heated to 75°, left standing at ambient temperature for 2 hr, poured into ice water, and filtered to give 1.0 g (59%) of **16**: a light yellow crystalline solid; mp 183–186°; ir (KBr) 1710 (C=O), 1325 and/or 1310, 1145 and/or 1140 cm$^{-1}$ ($SO_2$).

*Anal.* Calcd for $C_6H_5N_3O_3S_2$: N, 18.2; S, 27.7. Found: N, 17.9; S, 27.4.

**1-Methyl-3-(3-methylthiopyridazin-6-yl)urea (17).**—A suspension of 21.0 g (0.112 mol) of **14** and 7.9 g (0.112 mol) of sodium methylmercaptide in 100 ml of absolute methanol was stirred at 45° until a clear solution had formed (1 hr). After 18 hr the reaction mixture was poured into water and filtered to give 20 g of **15**, mp 141–144°. A suspension of 5 g (25 mmol) of **15** in 100 ml of 10% sodium hydroxide solution was placed on a steam bath for 30 min giving a clear solution. When a sample of this solution was acidified, hydrogen sulfide was liberated. After removal of water under reduced pressure, dimethylformamide and excess methyl isocyanate were added to the residual solid. After 24 hr this solution was diluted with water, and the product was filtered. Recrystallization from ethanol gave 1.0 g (20%) of **17**: a tan solid; mp 237–240°; ir (KBr) 3330, 3240 (NH), 1708 (C=O), 1555 and 1525 cm$^{-1}$ (amide II).

*Anal.* Calcd for $C_7H_{10}N_4SO$: C, 42.5; H, 5.0; N, 28.3; S, 16.2. Found: C, 42.6; H, 4.9; N, 28.6; S, 16.5.

**1-Methyl-3-(3-methylsulfonylpyridazin-6-yl)urea (18).**—A mixture of **17**, 0.5 g (2.25 mmol), in 20 ml of 33% hydrogen peroxide and 15 ml of acetic anhydride was heated at 80° for 2 hr, poured into ice water, filtered, and dried to give 0.6 g (90%) of

(14) M. Freund and C. Meinicke, *Ber.*, **29**, 2511 (1896); J. Goerdeler, J. Ohm, and O. Tegtmeier, *ibid.*, **89**, 1534 (1956).

(15) M. Busch and H. Biehler, *J. Prakt. Chem.*, [2] **93**, 339 (1916).

(16) J. Druey, K. Meier, and K. Eichenberger, *Helv. Chim. Acta*, **37**, 121 (1954).

(17) I. Lalezari and N. Shargki, *J. Heterocycl. Chem.*, **3**, 336 (1966).

(18) Y. Garceau, *C. R. Acad. Sci.*, **232**, 982 (1951).

(19) Solvent no. 3 (by volume): hexane (66), ethyl acetate (30), tetrahydrofuran (4). Solvent no. 9 (by volume): hexane (50), ethyl acetate (25), tetrahydrofuran (25). Solvent no. 10 (by volume): hexane (20), ethyl acetate (40), tetrahydrofuran (40).

18: a colorless crystalline solid; mp 257–260°; ir (KBr) 3330, 3250 (NH), 1710, 1700 (C=O), 1550 (amide II), 1350 or 1315, 1150 ($SO_2$).

*Anal.* Calcd for $C_7H_{10}N_4SO_3$: C, 36.5; H, 4.4; N, 24.4. Found: C, 36.4; H, 4.2; N, 23.9.

**Registry No.**—**1a**, 96-50-4; **1b**, 2289-75-0; **2a**, 2757-23-5; **2b**, 13221-50-6; **3** ($R^1$ = H; X = $SC_2H_5$), 38401-09-1; **4**, 38400-53-2; **5**, 38400-54-3; **6b**, 5319-77-7; **6c**, 25660-70-2; **6d**, 10444-89-0; **7**, 38400-58-7; **8**, 38400-59-8; **9**, 38400-60-1; **10**, 38400-61-2; **11**, 1072-98-6; **12**, 38400-63-4; **13**, 5469-69-2; **14**, 38400-66-7; **15**, 38400-67-8; **16**, 38400-65-6; **17**, 38400-68-9; **18**, 38400-69-0; **19**, 10416-84-9; **20**, 38400-71-4; sodium 2-amino-5-mercapto-1,3,4-thiadiazole, 38400-72-5; sodium methylmercaptide, 5188-07-8.

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# Bridgehead Nitrogen Heterocycles. III. Formation by Reaction of α-Ureido N-Heterocyclic Compounds with Chlorothioformyl Chloride

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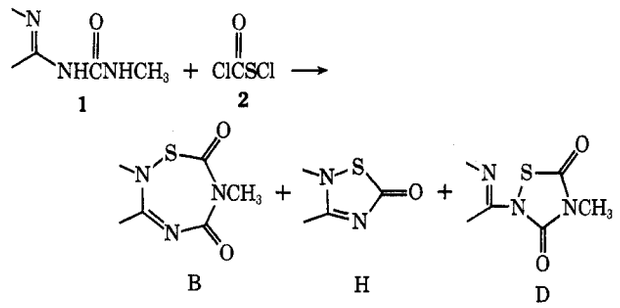
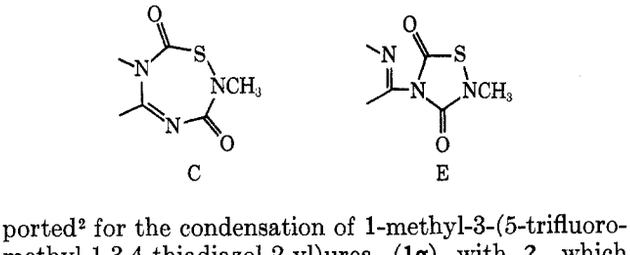
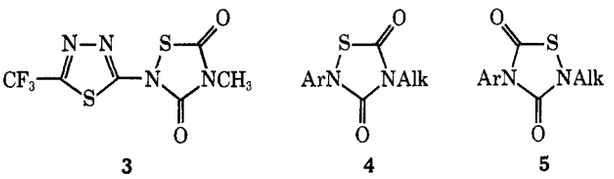
Condensation of α-ureido N-heterocyclic compounds (1) with chlorothioformyl chloride (2) is shown to give bicyclic bridgehead nitrogen heterocycles of general structure B and H as well as 2,4-disubstituted 1,2,4-thiadiazolidine-3,5-diones (D). The factors which control the course of the reaction and which determine the nature of the reaction product are discussed.

In the preceding article[1] it was shown that α-amino N-heterocyclic compounds (amidines) undergo reaction with chlorothioformyl chloride to give bicyclic bridgehead nitrogen heterocycles in fair yield. We now report the reactions of a series of α-ureido N-heterocyclic compounds (**1**) with chlorothioformyl chloride (**2**). Of



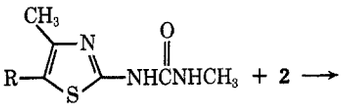
particular interest are the reactions of **2** with various **1** compounds in which the relative nucleophilicities of the exo- and endocyclic nitrogen atoms vary because theoretically these condensations can give fused thiatriazepinedione derivatives (*i.e.*, B and C) as well as 1,2,4-thiadiazolidinediones (*i.e.*, D and E). The result reported[2] for the condensation of 1-methyl-3-(5-trifluoromethyl-1,3,4-thiadiazol-2-yl)urea (**1g**) with **2**, which yielded 4-methyl-2-(5-trifluoromethyl-1,3,4-thiadiazol-2-yl)-1,2,4-thiadiazolidine-3,5-dione (**3**), does not indicate this variability in the direction of cyclization which can occur in these reactions. In agreement with the above result, however, it has been reported[3] that condensation of a series of 1-alkyl-3-arylureas yielded 4-alkyl-2-aryl-1,2,4-thiadiazolidine-3,5-diones (**4**); positional isomer **5** was not formed.



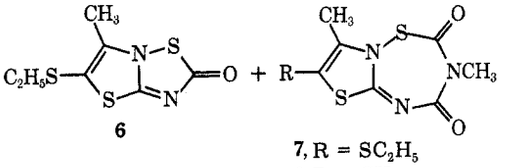


## Results and Discussion

When urea **1a** was allowed to react with **2** in xylene or *p*-dioxane in the presence of 2 molar equiv of triethylamine at 20–50°, there were obtained two compounds separated by silica chromatography and identified as 5-ethylthio-6-methyl-2*H*-thiazolo[3,2-*b*][1,2,4]-thiadiazol-2-one (**6**, 6.5%) and 3,8-dimethyl-7-ethylthio-2*H*-thiazolo[3,2-*b*][1,2,4,6]thiatriazepine-2,4(3*H*)-dione (**7**, 11.6%). However, when the reaction was carried out in refluxing xylene (4 hr), the only isolable product was **6** (6.5%); compound **7** could not be de-



**1a**, R = $SC_2H_5$
**b**, R = $CH_3$
**c**, R = $(CH_3)_2CHCH_2$



**7**, R = $SC_2H_5$
**8**, R = $CH_3$
**9**, R = $CH_2CH(CH_3)_2$

(1) K. Pilgram and R. D. Skiles, *J. Org. Chem.*, **38**, 1575 (1973).
(2) Farbenfabriken Bayer, A. G., Belgian Patent 746,833 (1970).
(3) G. Zumach and E. Kühle, *Angew. Chem.*, **82**, 63 (1970); *Angew. Chem., Int. Ed. Engl.*, **9**, 54 (1970).