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.

**Acknowledgment.**—We are indebted to Dr. S. B. Soloway for his constant encouragements and to Drs. B. C. Baker, W. J. McKinney, and G. E. Pollard for microanalyses and spectral measurements.

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

KURT PILGRAM* AND RICHARD D. SKILES

*Biological Sciences Research Center, Shell Development Company, Modesto, California 95352*

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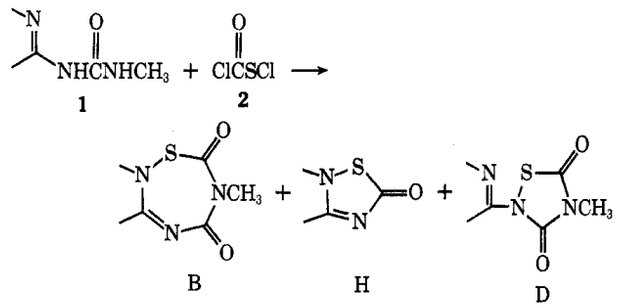
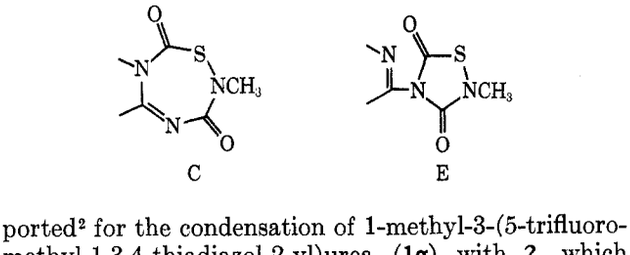
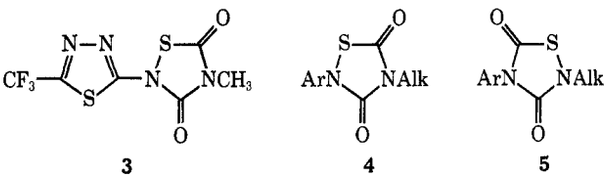
Condensation of α-ureido N-heterocyclic compounds (1) with chlorothioformyl chloride (2) is shown to give bicyclic bridgehead nitrogen heterocycles of general structure B and H as well as 2,4-disubstituted 1,2,4-thiadiazolidine-3,5-diones (D). The factors which control the course of the reaction and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



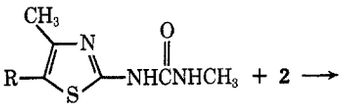
particular interest are the reactions of **2** with various **1** compounds in which the relative nucleophilicities of the exo- and endocyclic nitrogen atoms vary because theoretically these condensations can give fused thiatriazepinedione derivatives (*i.e.*, B and C) as well as 1,2,4-thiadiazolidinediones (*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.



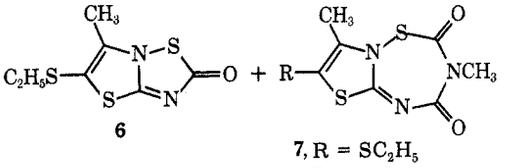


## Results and Discussion

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).

TABLE I

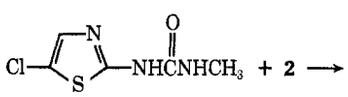
HETEROCYCLES OBTAINED BY REACTION OF α-UREIDO N-HETEROCYCLIC COMPOUNDS (1) WITH CHLOROTHIOFORMYL CHLORIDE (2)[a]

| Compd | Yield, % | Mp, °C | Formula | Nmr Data, δ[b] | Solvent |
|---|---|---|---|---|---|
| 6 | 6.5 | 78–81 | $C_7H_8N_2OS_3$ | 1.3 (t, 3, $CH_3CH_2$), 2.8 (q, 2, $CH_3CH_2$) | $CDCl_3$ |
| 7 | 11.6 | 57–58 | $C_9H_{11}N_3O_2S_3$ | 1.3 (t, 2, $CH_3CH_2$), 2.85 (q, 2, $CH_3CH_2$), 2.2 (s, 3, $CH_3C$=), 3.3 (s, 3, $NCH_3$) | $CDCl_3$ |
| 8 | 25 | 154–156 | $C_6H_9N_3O_2S_2$ | 2.25 (d, 3, 7-$CH_3$), 2.35 (d, 3, 8-$CH_3$), 3.15 (s, 3, $NCH_3$) | DMSO-$d_6$ |
| 9 | 63 | Oil | $C_{11}H_{15}N_3O_2S_2$ | 1.0 [d, 6, $(CH_3)_2$], 2.0 (m, 1, CH), 2.35 (s, 3, $CH_3C$=), 2.65 (d, 2, $CH_2$), 3.2 (s, 3, $NCH_3$) | $CDCl_3$ |
| 10 | 34 | 132–133 | $C_4HClN_2OS_2$ | 7.2 (s, CH=) | $CDCl_3$ |
| 11 | 4.3 | 139–141 | $C_6H_4ClN_3O_2S_2$ | 7.6 (s, 1, CH=), 3.3 (s, 3, $NCH_3$) | $CDCl_3$ |
| 12 | 25 | 210 dec | $C_3HN_3OS_2$ | | |
| 13 | 63 | 149–152 | $C_4H_3N_3OS_2$ | 2.75 (s, $SCH_3$) | $CDCl_3$ |
| 3 | 50 | 98–100 | $C_6H_3F_3N_4O_2S_2$ | 7.0 (m, 4, $C_6H_4$), 3.3 (s, 3, $NCH_3$) | $CDCl_3$ |
| 16 | 60 | 162–165 | $C_5H_2ClN_3OS$ | 7.45 (q, 1, CH=), 7.9 (q, 1, CH=) | DMSO-$d_6$ |

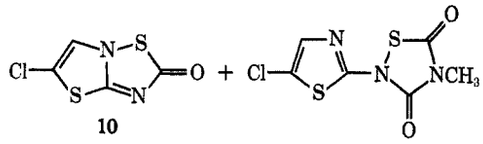
[a] Satisfactory analytical data (±0.3% for C, H, and N) were reported for all compounds in this table; S analyses were reported for all except 6, 7, and 12; Cl analyses were reported for 10 and 11. [b] In parts per million (multiplicity, number of protons, assignment).

tected (tlc) in the reaction mixture. The two ureas **1b** and **1c** reacted with **2** to give the fused thiatriazepinedione derivatives **8** (25%) and **9** (63%), and no further reaction products could be detected in the reaction mixture.

The reaction mixture obtained by treatment of **1d** with **2** in refluxing benzene (18 hr) contained two products which were separated by column chromatography and identified as 5-chloro-2*H*-thiazolo[3,2-*b*]-[1,2,4]thiadiazol-2-one (**10**, 34%) and 2-(5-chlorothiazol-2-yl)-4-methyl-1,2,4-thiadiazolidine-3,5-dione (**11**, 4.3%).



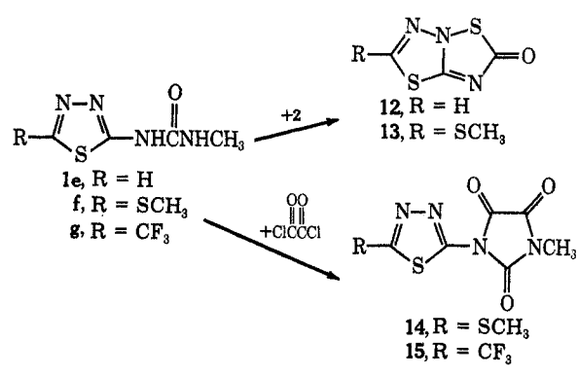
**1d**



**10** **11**

The ureas **1e**, **1f**, and **1g** were allowed to condense with **2** in refluxing benzene or *p*-dioxane in the presence or absence of triethylamine to determine whether or not the direction of cyclization would be the same as with **1d** and **2**. The results of these three experiments indicated that the cyclizations occurred similarly to give either a 2*H*-1,3,4-thiadiazol[3,2-*b*][1,2,4]thiadiazol-2-one (**12**, 25%) and **13** (63%) or a 2,4-disubstituted 1,2,4-thiadiazolidine-3,5-dione derivative (**3**, 50%). Surprisingly, the reactions of both **1f** and **1g** with oxalyl chloride which were effected in refluxing xylene resulted in almost quantitative (94–98%) yields of the parabanic acid derivatives **14** and **15** (Scheme I); fused compounds analogous to **13** could not be detected. Compound **13** was identical (elemental analysis, melting point, mixture melting point, ir and nmr spectrum, and formation of an identical sulfone) with the product obtained earlier[1] in 10% yield as a result of the interaction of 2-amino-5-methylthio-1,3,4-thiadiazole with **2** in the presence of 2 molar equiv of triethylamine.

SCHEME I

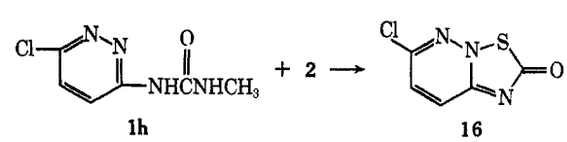


**12**, R = H
**13**, R = $SCH_3$

**1e**, R = H
**f**, R = $SCH_3$
**g**, R = $CF_3$

**14**, R = $SCH_3$
**15**, R = $CF_3$

The reaction of **1h** with **2** proceeded smoothly in refluxing xylene (18 hr) to give 6-chloro-2*H*-[1,2,4]-thiadiazolo[2,3-*b*]pyridazin-2-one (**16**) in 60% yield.



**1h** **16**

The identity of this compound with that obtained by reaction of 3-amino-6-chloropyridazine with **2**[1] was verified (elemental analysis, melting point, mixture melting point, nmr, and mass spectrum).

Table I lists data of compounds **3**, **6**–**13**, and **16**.

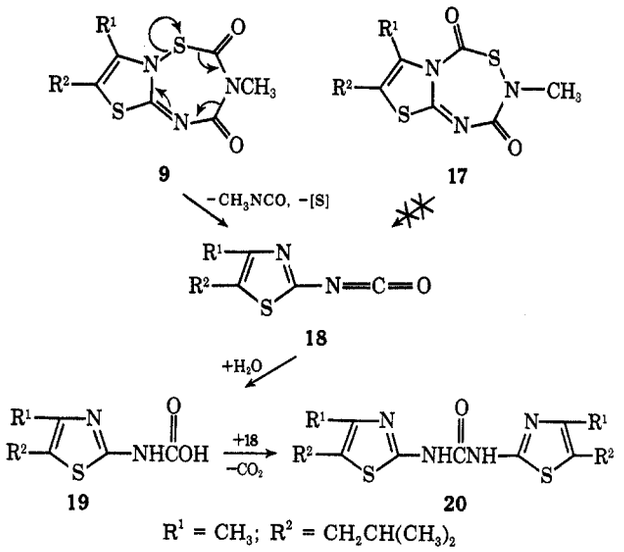
The identification of **7**, **8**, and **9** as thiatriazepinediones of general structure B is based upon the following observations. Elemental analyses indicate that ring closure occurred. Structure B is preferred over that of C, D, and E on chemical and spectroscopic grounds. Compounds of general structure D are thermally stable.[3,4] Compounds **7**, **8**, and **9** on the other hand undergo facile decomposition with elimination of methyl isocyanate and sulfur when heated or stored at ambient temperature over extended periods of time. In this respect, the behavior of these compounds resembles that of annelated 3-phenyl-1,3,5-triazine-2,4-diones which eliminate phenyl isocyanate on heating.[5]

(4) G. Zumach, L. Eue, W. Weiss, E. Kühle, and H. Hack, South African Patent 67/07491 (1968) [*Chem. Abstr.*, **70**, 47465r (1969)]; British Patent 1,115,350 (1968) [*Chem. Abstr.*, **69**, 96732p (1968)].

(5) U. v. Gizycki and G. Oertel, *Angew. Chem.*, **80**, 363 (1968); *Angew. Chem., Int. Ed. Engl.*, **7**, 381 (1968).

When **9** was exposed to moist air at 60° in a vacuum oven for 72 hr, the urea **20** was isolated in 50% yield in addition to elemental sulfur. The mechanism postulated to account for this mode of fragmentation is illustrated in Scheme II. A positional isomer such as **17**

SCHEME II



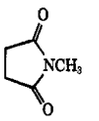
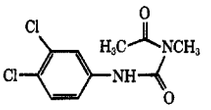
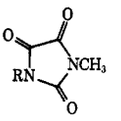
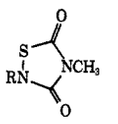
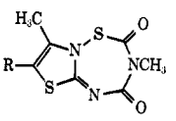

which has also been considered as the product from **1c** and **2** (*e.g.*, C), would not be expected to fragment readily to **18**. Water may intercept the unstable **19** to give the carbamic acid **21** which by loss of carbon dioxide[6] and addition to **19** gives the symmetrical urea **20**. In the absence of hydroxylic solvents, **18** would be expected to cyclodimerize.[5]

The $NCH_3$ chemical shift is predictive of whether the cyclization products derived from **1** with **2** have general structures B and D or C and E. For example, in nitrogen heterocycles, one or two carbonyl groups adjacent to the nitrogen atom have a pronounced effect on the nmr chemical shift of the substituent on the nitrogen atom; *e.g.*, in *N*-methylpyrrolidine[7] the chemical shift of the methyl group is $\delta$ 2.33 ppm. In *N*-methylpyrrolidone[7] and *N*-methylsuccinimide the corresponding chemical shifts are $\delta$ 2.82 and 3.00 ppm, respectively. The nmr data for the various cyclization products derived from **1** and **2** are consistent with those for heterocycles containing similar arrangements (Table II). The chemical shift of the *N*-methyl group is invariably observed at $\delta$ 3.15–3.33 ppm indicating the presence of the $-C(=O)N(CH_3)C(=O)-$ grouping in heterocycles such as **3**, **7**, **8**, **9**, and **11**.

The thiatriazepinedione cyclization products derived from **1** with **2** were further characterized by their ir spectra; peaks in the ir were assigned in the light of well-established correlations of C=O groups. Iminocarbonyl groups which are part of a ring system have C=O bands at 1790–1720 and 1710–1670 $cm^{-1}$,[8] the lower frequency band being more intense. In conformity with general structure B, the compounds **7**, **8**, and **9** show two characteristic carbonyl bands at 1758–1741 and 1705–1695 $cm^{-1}$ of which the higher frequency band

(6) C. W. van Hoogstraten, *C. R. Acad. Sci.*, **51**, 414 (1932).
(7) J. C. N. Ma and E. W. Warnhoff, *Can. J. Chem.*, **43**, 1849 (1965).
(8) L. J. Bellamy, "Advances in Infrared Frequencies," Vol. 130, Methuen and Co. Ltd., London, 1968, p 134.

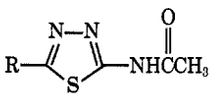
TABLE II
NUCLEAR MAGNETIC RESONANCE POSITIONS FOR *N*-METHYL GROUPS

| Compd | Structure | $\delta$ in $CDCl_3$ (ppm) |
|---|---|---|
| |  | 2.33[a] |
| |  | 2.82[a] |
| |  | 3.00 |
| **23** |  | 3.35 |
| **15, 16** |  | 3.1–3.2[b] |
| **11, 14** |  | 3.30–3.33 |
| **7, 8, 9** |  | 3.15–3.30 |

[a] Reference 7. [b] In DMSO-$d_6$.

is weaker in intensity. Similarly, compounds of general structure D (*e.g.*, **3** and **11**) have two C=O bands at 1765–1740 and 1730–1710 $cm^{-1}$.

As depicted in Scheme III, the formation of H (*e.g.*, **6**, **10**, **12**, **13**, and **16**), which poses an interesting mechanistic problem, can be rationalized as proceeding *via* the corresponding $\alpha$-amino N-heterocyclic compound, F. As these reactions of **1** with **2** leading to H are carried out at elevated temperature, the intermediate formation of F from **1** by loss of methyl isocyanate is not unexpected in view of the fact that almost all monomethylureas show the tendency to give off methyl isocyanate at elevated temperature.[9] For example, when **1f** and **1g** were treated with acetyl chloride in refluxing xylene or at 80° in the presence or absence of triethylamine, the corresponding acetamides **21** and **22** were isolated in fair (50%) yield.



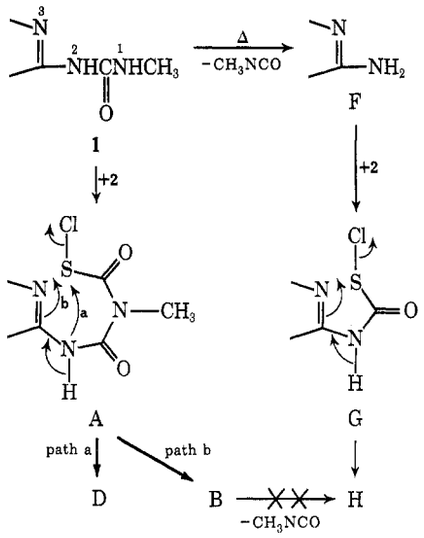
**21**, R = $SCH_3$
**22**, R = $CF_3$

The thermally unstable thiatriazepinedione B is not a precursor of H as evidenced by the failure to detect H (*e.g.*, **6**) in a refluxing solution of B (*e.g.*, **7**) in xylene. The formation of B and D is presumed to arise *via* the acylated urea A. Because $N^1$ (bearing a methyl group) is a better nucleophile than $N^2$ (exocyclic nitrogen) and

(9) S. Petersen, *Justus Liebigs Ann. Chem.*, **562**, 205 (1949).

$N^3$ (endocyclic nitrogen) for acylation,[10] the condensation should proceed through intermediate A to give B and D *via* the respective pathways a and b (Scheme III).

SCHEME III




Intermediate products arising from initial N-sulfenylation may be excluded from consideration on grounds previously discussed.[1]

In summary, the reactions of α-ureido N-heterocyclic compounds with chlorothioformyl chloride provide a convenient way to a variety of 2,3-fused 1,2,4,6-thiatriazepine-5,7-diones (B) 2,3-fused 1,2,4-thiadiazolin-5-ones (H), and 2,4-disubstituted 1,2,4-thiadiazolidine-3,5-diones (D).

## Experimental Section

The usual general remarks[1] regarding apparatus are applicable.

**Materials.**—Procedures for the preparation of monomethylureas are well documented in the literature.[12] With the exception of **1d**, all other ureas were prepared from methyl isocyanate and the respective α-amino N-heterocyclic compound. Urea **1d** was obtained in 32% yield by chlorination with sulfuryl chloride of 1-methyl-3-(thiazol-2-yl)urea following a literature procedure.[13] Physical and analytical data of ureas prepared in context with the present work as precursor of novel heterocyclic compounds are listed in Table III.

**5-Ethylthio-6-methyl-2*H*-thiazolo[3,2-*b*][1,2,4]thiadiazol-2-one (6) and 3,8-dimethyl-7-ethylthio-2*H*-thiazolo[3,2-*b*][1,2,4,6-]thiatriazepine-2,4(3*H*)-dione (7).**—To a slurry of 19.9 g (86 mmol) of **1a** in 125 ml of xylene was added dropwise with stirring 12.5 g (95 mmol) of **2**, causing the temperature to rise from 20 to 25°. To this mixture was added dropwise a solution of 19.0 g (188 mmol) of triethylamine in 75 ml of xylene. After 24 hr, the reaction mixture was washed with water, dried ($MgSO_4$), and evaporated to dryness under reduced pressure. Separation by silica chromatography[14] of the residue gave 1.3 g (6.5%) of **6**: a light yellow crystalline solid; mp 78–81° (from hexane); ir (KBr) 1595 (C=), 1690 $cm^{-1}$ (C=O); mass spectrum (70 eV) 232 ($M^+$). The second compound, 2.9 g (11.6%) of colorless solid, was identified as **7**: mp 57–58° (from hexane); ir ($CH_2Cl_2$) 1705, 1755 $cm^{-1}$ (C=O).

In another experiment, a mixture of 15.5 g (67 mmol) of **1a** and 9.7 g (74 mmol) of **2** in 100 ml of xylnee was heated to reflux (4 hr). The reaction gave off hydrogen chloride and turned dark. The solvent was removed under reduced pressure and the residual black tar was purified by silica chromatography to give 1.0 g (6.5%) of **6**, identical with the product obtained above.

**5-Chloro-2*H*-thiazolo[3,2-*b*][1,2,4]thiadiazol-2-one (10) and 2-(5-Chlorothiazol-2-yl)-4-methyl-1,2,4-thiadiazolidine-3,5-dione (11).**—A suspension of 9.0 g (47 mmol) of **1d** in 100 ml of benzene and 6.9 g (52 mmol) of **2** was heated to reflux until hydrogen evolution ceased (18 hr). The solvent was removed and the residual solid was purified by silica chromatography to give 4.0 g (34%) of **10** [a colorless crystalline solid; mp 132–133° (from methanol); ir ($CH_2Cl_2$) 1720, 1690 $cm^{-1}$ (C=O)] and 0.5 g (4.3%) of **11** [a tan crystalline solid; mp 139–141°; ir ($CH_2Cl_2$) 1740, 1710 $cm^{-1}$ (C=O)].

**2-Methylthio-6*H*-[1,3,4]thiadiazolo[3,2-*d*][1,2,4]thiadiazol-6-one (13).**—A mixture of 8.0 g (39.2 mmol) of **1f**, 100 ml of toluene, and 5.8 g (44 mmol) of **2** was stirred and heated at reflux for 18 hr. The solvent was removed and the residual solid was recrystallized from methanol to give 5.0 g (63%) of **13**: a tan solid; mp 149–152°; ir ($CH_2Cl_2$) 1730, 1713, 1690 $cm^{-1}$ (C=O). Oxidation with *m*-chloroperbenzoic acid in chloroform solution afforded a sulfone, mp 145–148°, identical (mixture melting point, ir, nmr) with the product obtained by reaction of **2** with 2-amino-5-methylthio-1,3,4-thiadiazole.[1]

**1-Methyl-3-(5-methylthio-1,3,4-thiadiazol-2-yl)imidazolidinetrione (14).**—A solution of 9.0 g (44.2 mmol) of **1f** and 6.2 g (48.6 mmol) of oxalyl chloride in 150 ml of toluene was refluxed for 18 hr. Recrystallization of the solid product from methanol gave 5.5 g (94%) of **14**: a cream-colored solid; mp 172–174°; ir (KBr) 1750 $cm^{-1}$ (C=O); nmr (DMSO-$d_6$) δ 2.8 (s, 3, $SCH_3$), 3.1 ppm (s, 3, $NCH_3$).

*Anal.* Calcd for $C_7H_6N_4O_3S_2$: C, 32.6; H, 2.3; N, 21.7; S, 24.8. Found: C, 33.0; H, 2.4; N, 22.0; S, 24.9.

**1-Methyl-3-(5-methylsulfonyl-1,3,4-thiadiazol-2-yl)imidazolidinetrione.**—A solution of 4.5 g (22.4 mmol) of **14** and 9.1 g of 85% *m*-chloroperbenzoic acid (44.8 mmol) in 100 ml of chloroform was refluxed for 18 hr and, after filtration, washed with aqueous sodium carbonate and with water, dried ($MgSO_4$), and evaporated to dryness. Recrystallization from methanol afforded 5.0 g (77%) of a colorless crystalline solid: mp 247–250°; ir (KBr) 1740 (C=O), 1320 and 1160 ($SO_2$); nmr (DMSO-$d_6$) δ 3.15 (s, 3, $NCH_3$), 3.7 ppm (s, 3, $SO_2CH_3$).

*Anal.* Calcd for $C_7H_6N_4O_5S_2$: C, 29.0; H, 2.1; N, 19.3. Found: C, 29.2; H, 2.3; N, 19.2.

**3-Methyl-1-(5-trifluoromethyl-1,3,4-thiadiazol-2-yl)imidazolidinetrione (15).**—To a solution of 10.0 g (44.2 mmol) of **1g** in 100 ml of toluene was added with stirring 6.2 g (48.6 mmol) of oxalyl

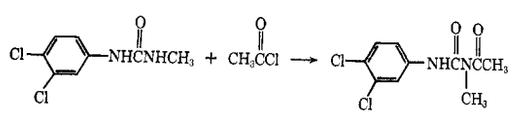
TABLE III

α-UREIDO N-HETEROCYCLIC COMPOUNDS, RNHC(=O)NHCH$_3$[a]

| Compd | Yield, % | Mp, °C | Formula |
|---|---|---|---|
| **1a** | 61 | 178–180, 188–190 | $C_8H_{13}N_3OS_2$ |
| **1b** | 70 | 182–184 | $C_7H_{11}N_3OS$ |
| **1c** | 58 | 183–185 | $C_{10}H_{17}N_3OS$ |
| **1d** | 32 | 242 | $C_5H_6ClN_3OS$ |
| **1e** | 85 | 232 | $C_4H_6N_4OS$ |
| **1f** | 52 | 205–210 | $C_5H_8N_4OS_2$ |
| **1g** | 92 | 192–194 | $C_5H_5F_3N_4OS$ |
| **1h** | 82 | 257–259 | $C_6H_7ClN_4O$ |

[a] Satisfactory analytical data (±0.3% for C and H) were reported for **1a**, **1b**, **1c**, **1g**, and **1h**; N analyses were reported for all except **1h**; S analyses were reported for **1e**, **1f**, and **1g**; Cl analyses were reported for **1d** and **1h**.

(10) For example, acetylation of 1-methyl-3-(3,4-dichlorophenyl)urea led to 1-acetyl-1-methyl-3-(3,4-dichlorophenyl)urea (**23**) as the only isolable reaction product. An authentic specimen of **23**[11] proved to be identical (melting point, mixture melting point, tlc, glc, and nmr and ir spectrum) with the above product.




**23**

(11) H. J. Gerjovich and R. S. Johnson, U. S. Patent 2,762,696 (1957) [*Chem. Abstr.*, **51**, 3911 (1957)].

(12) S. Petersen, "Die Methoden der organischen Chemie" (Houben-Weyl), Vol. 8, E. Müller, Ed., Georg Thieme Verlag, Stuttgart, Germany, 1952, p 157.

(13) E. Pedley, *J. Chem. Soc.*, 431 (1947).

(14) Solvent mixture (by volume): Tetrahydrofuran (2) and hexane (48).

chloride. This solution was haeted to reflux for 18 hr. Hydrogen chloride evolved during the first 3 hr. The reaction mixture was filtered while hot and cooled to give 9.0 g (98%) of **15**: an off-white solid; mp 258–261°; ir (KBr) 1790, 1760, and 1730 (C=O), 1340, 1160, and 1145 $cm^{-1}$ ($CF_3$); nmr (DMSO-$d_6$) $\delta$ 3.2 ppm (s, $NCH_3$).

*Anal.* Calcd for $C_7H_3F_3N_4O_3S$: C, 30.0; H, 1.1; N, 20.0; S, 11.4. Found: C, 30.3; H, 1.0; N, 20.1; S, 11.1.

**6-Chloro-2*H*-[1,2,4]thiadiazolo[2,3-*b*]pyridazin-2-one (16).**—A mixture of 15.0 g (0.805 mol) of **1h** and 11.0 g (0.805 mol) of **2** in 100 ml of xylene was heated to reflux (18 hr), evaporated, and recrystallized from methanol (charcoal) to give 9.0 g (60%) of **16**, a light yellow crystalline solid, mp 162–165°, identical (mixture melting point, ir, nmr) with a product obtained by reaction of **2** with 3-amino-6-chloropyridazine.[1]

**1,3-Bis(5-isobutyl-4-methylthiazol-2-yl)urea (20).**—A slow stream of air was passed at 60° over a 1.0-g (3.5 mmol) sample of **9**. After 72 hr, the product was washed with acetone and then with ether to give 0.3 g (50%) of **20**: a tan solid; mp 180–215° dec; ir (KBr) 3400, 2400 (NH), 1700, 1625 (C=), 1540 $cm^{-1}$ (amide II); mass spectrum (70 eV), 366 ($M^+$), 323, 197, 196, 171, 170, 153, 127, 100, 85, 76, 73, 69, 64, 59, 57, 44–41.

*Anal.* Calcd for $C_{17}H_{26}N_4OS_2$: C, 55.6; H, 7.1; N, 15.3. Found: C, 55.8; H, 7.1; N, 15.3.

***N*-(5-Methylthio-1,3,4-thiadiazol-2yl)acetamide (21). A. By Reaction of 1f with Acetyl Chloride.**—A mixture of 20.4 g (0.1 mol) of **1f**, 12.0 g (0.15 mol) of acetyl chloride, and 150 ml of xylene was refluxed with stirring for 24 hr. The product obtained after cooling and filtration was recrystallized from aqueous methanol to give 9.0 g (48%) of **21**: a tan solid; mp 209–212°; ir (KBr) 3160 (NH), 1709 (C=O), 1560 $cm^{-1}$ (amide II); nmr (DMSO-$d_6$) $\delta$ 2.2 (s, 3, $CH_3CO$), 2.7 (s, 3, $CH_3S$), 12.45 ppm (s, 1, NH); mass spectrum (70 eV) 189 ($M^+$), 174 ($M - CH_3$), 147, 111, 97, 95, 85, 83, 71, 69, 57, 43, 27, 18.

*Anal.* Calcd for $C_5H_7N_3S_2O$: C, 31.8; H, 3.7; N, 22.2. Found: C, 31.8; H, 3.6; N, 22.4.

**B. By Reaction of 1f with Acetyl Chloride in the Presence of Triethylamine.**—To a solution of 20.4 g (0.1 mol) of **1f** and 10.1 g (0.1 mol) of triethylamine in 150 ml of *p*-dioxane was added with stirring 8.6 g (0.11 mol) of acetyl chloride. After 18 hr at ambient temperature, only starting material (**1f**) could be detected by tlc. The mixture was heated at 80° for 1.5 hr, evaporated to dryness, washed with water, and recrystallized from aqueous methanol (1:1) to give 8.5 g (46.3%) of **21**, mp 209–212°; a mixture melting point with the product obtained by method A was undepressed.

**C. By Reaction of 2-Amino-5-methylthio-1,3,4-thiadiazole with Acetic Anhydride.**—A solution of 2.7 g (18.5 mmol) of 2-amino-5-(methylthio)-1,3,4-thiadiazole[15] in 50 ml of acetic anhydride was heated to reflux for 2.5 hr, poured into 300 ml of water, and stirred for 3 hr. The solid was filtered, washed with water, and dried to give 3.0 g (86%) of **21**, a tan solid, mp 209–212°; a mixture melting point with the product obtained by method A was undepressed.

***N*-(5-Trifluoromethyl-1,2,4-thiadiazol-2-yl)acetamide (22).**—A solution of 5.05 g (22.1 mmol) of **1g** and 3.0 g (38.5 mmol) of acetyl chloride in 75 ml of xylene was refluxed for 2 hr. Cooling to 10° gave 2.5 g (58%) of **22**: a light tan crystalline solid; mp 235°; nmr (DMSO-$d_6$) $\delta$ 2.25 (s, 3, $CH_3$), 13.25 ppm (s, 1, NH).

*Anal.* Calcd for $C_5H_4F_3N_3SO$: C, 28.5; H, 1.9; N, 19.9. Found: C, 28.6; H, 2.0; N, 20.2.

**1-Acetyl-3-(3,4-dichlorophenyl)-1-methylurea (23).**—A mixture of 3-(3,4-dichlorophenyl)-1-methylurea (5.5 g, 25 mmol), triethylamine (2.5 g, 25 mmol), and acetyl chloride (2.0 g, 25 mmol) in 75 ml of xylene was heated in a sealed glass cylinder on a steam bath for 18 hr. The reaction mixture was evaporated and the residue was washed with water and recrystallized from benzene to give 1.5 g (23%) of colorless crystalline solid: mp 144–146°; nmr ($CDCl_3$) $\delta$ 2.35 (s, 3, $CH_3CO$), 3.55 (s, 3, $CH_3N$), 7.4–7.7 (m, 3, $C_6H_3$), 11.6 ppm (s, 1, NH); ir (KBr) 1715 (C=O), 1550 $cm^{-1}$ (amide II); mixture melting point was authentic[11] **23** undepressed.

*Anal.* Calcd for $C_{10}H_{10}N_2O_2Cl_2$: C, 46.0; H, 3.8; N, 10.7; Cl, 27.2. Found: C, 46.1; H, 4.0; N, 10.4; Cl, 27.2.

**Registry No.**—**1a**, 34006-36-5; **1b**, 14934-65-7; **1c**, 38401-12-6; **1d**, 14953-32-6; **1e**, 26676-41-5; **1f**, 25958-19-4; **1g**, 25366-20-5; **1h**, 38401-17-1; **2**, 2757-23-5; **3**, 28924-68-7; **6**, 38401-20-6; **7**, 38401-21-7; **8**, 38401-22-8; **9**, 38401-23-9; **10**, 38401-24-0; **11**, 38401-25-1; **12**, 38401-26-2; **13**, 38400-58-7; **14**, 28924-66-5; **15**, 28924-65-4; **16**, 38400-66-7; **20**, 38401-31-9; **21**, 38583-51-6; **22**, 10444-99-2; **23**, 38401-33-1; oxalyl chloride, 79-37-8; 1-methyl-3-(5-methylsulfonyl-1,3,4-thiadiazol-2-yl)imidazolidinetrione, 28924-64-3; *m*-chloroperoxybenzoic acid, 937-14-4; acetyl chloride, 75-36-5; 2-amino-5-methylthio-1,3,4-thiadiazole, 5319-77-7; acetic anhydride, 108-24-7; 3-(3,4-dichlorophenyl)-1-methylurea, 3567-62-2.

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