Chemistry of 1,2,3,4-Thiatriazoles. Synthesis of 3-Oxo-Δ^4-1,2,4-thiadiazolin-5-yl Ureas

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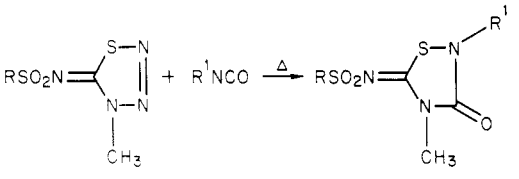
The reaction of 5-amino-1,2,3,4-thiatriazoles with isocyanates was found to give 3-oxo-Δ^4-1,2,4-thiadiazolin-5-yl ureas. The structures were verified by independent synthesis and ^1H and ^{13}C spectroscopy.

The reactions of the 1,2,3,4-thiatriazoles have been studied only to a limited degree after the structure of the ring system was firmly established in 1957.[1] The pertinent chemistry, much of it being thermal decomposition studies of the fairly labile ring, has been reviewed by Jensen[2,3] and by Holm.[4]

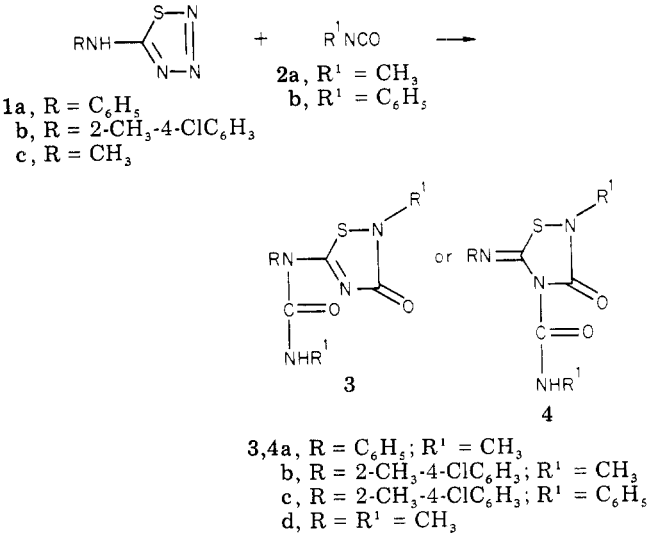
The known reactions of the 5-amino-1,2,3,4-thiatriazoles are even more limited, consisting of rearrangements and decomposition under basic and acidic conditions, acylation on the 5-amino nitrogen, and alkylation in the 4 position or on 5-amino nitrogen.[3,4]

During the last several years, a large amount of work has been done with the related 4-alkyl-5-imino-1,2,3,4-thiatriazolines. Thus, Neidlein et al. synthesized 4-methyl-5-(arylimino)-1,2,3,4-thiatriazolines[5] and 4-methyl-5-(arylsulfonylimino)-1,2,3,4-thiatriazolines[6] and decomposed them at elevated temperatures (90–120 °C) to generate reactive intermediates, which undergo intramolecular cyclization[5] or add to cumulative double bonds.[6]



Similarly, L'abbé et al. examined the analogous decomposition–addition of 4-alkyl-5-(sulfonylimino)-1,2,3,4-thiatriazolines in the presence of enamines, ynamines, keto-stabilized phosphorus ylides, imines, nitriles, ketenes, isocyanates, carbodiimides, and isothiocyanates at moderate temperatures (60–80 °C)[7-10a] and more recently the reactions of 4-alkyl-5-(arylimino)-1,2,3,4-thiatriazolines with acyl isothiocyanates and sulfenes[10b] and with isocyanates[10c] at room temperature. Toubro and Holm[10d] have recently described the analogous reaction of the 4-alkyl-5-(alkylimino) derivatives with ketenes.

Scheme I

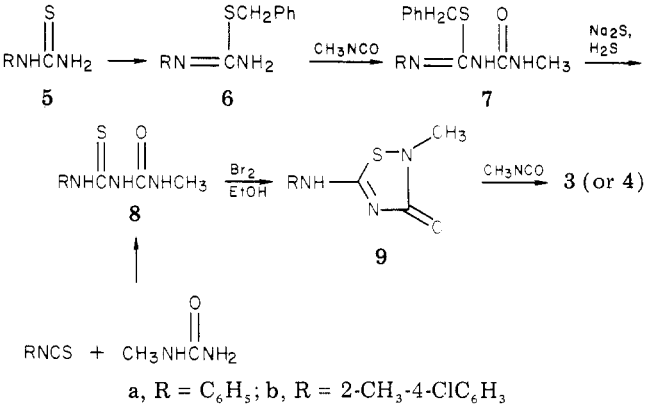


1a, R = C_6H_5
b, R = 2-CH_3-4-ClC_6H_3
c, R = CH_3

2a, R^1 = CH_3
b, R^1 = C_6H_5

3,4a, R = C_6H_5; R^1 = CH_3
b, R = 2-CH_3-4-ClC_6H_3; R^1 = CH_3
c, R = 2-CH_3-4-ClC_6H_3; R^1 = C_6H_5
d, R = R^1 = CH_3

Scheme II



a, R = C_6H_5; b, R = 2-CH_3-4-ClC_6H_3

We now wish to report the first example[11] of a similar reaction with the parent ring system; namely, 5-amino-1,2,3,4-thiatriazoles with isocyanates. The reactions occur rapidly at room temperature and lead to 3-oxo-Δ^4-1,2,4-thiadiazolines.

Results and Discussion

Initially, the reaction of 5-anilino-1,2,3,4-thiatriazole (**1a**) with methyl isocyanate was examined. It became obvious that the reaction was not a simple urea formation when

(1) E. Lieber, C. N. Pillai, and R. D. Hites, *Can. J. Chem.*, **35**, 832 (1957).
(2) K. A. Jensen and C. Pedersen, *Adv. Heterocycl. Chem.*, **3**, 263 (1964).
(3) K. A. Jensen, *Z. Chem.*, **9**, 121 (1969).
(4) A. Holm, *Adv. Heterocycl. Chem.*, **20**, 145 (1976).
(5) R. Neidlein and J. Tauber, *Arch. Pharm. (Weinheim, Ger.)*, **304**, 687 (1971).
(6) R. Neidlein and K. Salzman, *Synthesis*, 52 (1975).
(7) E. VanLoock, J. M. Vandensavel, G. L'abbé, and G. Smets, *J. Org. Chem.*, **38**, 2916 (1973).
(8) G. L'abbé, E. VanLoock, R. Albert, S. Toppet, G. Verhelst, and G. Smets, *J. Am. Chem. Soc.*, **96**, 3973 (1974).
(9) G. L'abbé, G. Verhelst, C.-C. Yu, and S. Toppet, *J. Org. Chem.*, **40**, 1728 (1975).
(10) (a) G. L'abbé, G. Verhelst, and S. Toppet, *J. Org. Chem.*, **41**, 3403 (1976); (b) G. L'abbé, A. Timmerman, C. Martens, and S. Toppet, *ibid.*, **43**, 4951 (1979); (c) G. L'abbé and G. Verhelst, *Angew. Chem., Int. Ed. Engl.*, **15**, 489 (1976); (d) N. H. Toubro and A. Holm, *J. Chem. Soc., Perkin Trans. 1*, 1440 (1978).

(11) We thank one of the referees for providing a reference to a brief publication [R. J. S. Beer and I. Hart, *J. Chem. Soc., Chem. Commun.*, 143 (1977)] in which the reaction of 1 (R=H) with **2b** is described but the product is not identified.

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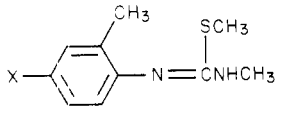
gas evolution was observed, and analysis showed that 2 equiv of methyl isocyanate were incorporated and N_2 was lost. The reaction was complete at room temperature in 1 or 2 days. In the presence of a catalytic amount of triethylamine, nitrogen evolution was very fast; the reaction was exothermic and went to completion in a few hours. The product was postulated to have structure **3a** or **4a** as shown in Scheme I on the basis of elemental analysis, by spectral evidence, and by analogy to previous work.[6,8]

A consideration of possible reaction pathways leads to other structures as well. However, the 3-oxo-1,2,4-thiadiazoline ring structure **9** in the product was confirmed by independent synthesis of **9a** and **9b** as shown in Scheme II. Thus, the other possible structures were excluded, but since either **3** or **4** could be formed via this scheme, only the structure of the parent ring system was established.

The syntheses of **9a** and **9b** were uneventful. The structure of **8** was defined by its synthesis via the two indicated methods, which can only give one common product; namely, **8**. Oxidative cyclization gave **9**, which was extremely insoluble in organic solvents but even so reacted rapidly with methyl isocyanate to give **3** (or **4**).

Convincing evidence that **3** was the correct structure was provided by ^{13}C NMR. From the recent work of Olah and Donovan,[12] a ^{13}C additivity factor[13] of δ 24.8 can be calculated for C_1 of a phenylimino group in Schiff bases. A slightly smaller factor of δ 20.0 (range 19.4 to 20.7) for the C_1 of the phenylimino group in the more closely related thiopseudoureas was calculated from the ^{13}C NMR data of three 1-(2-methyl-4-X-phenyl)-2,3-dimethyl-2-thiopseudoureas **10**, where X is methyl, chloro, or nitro. The



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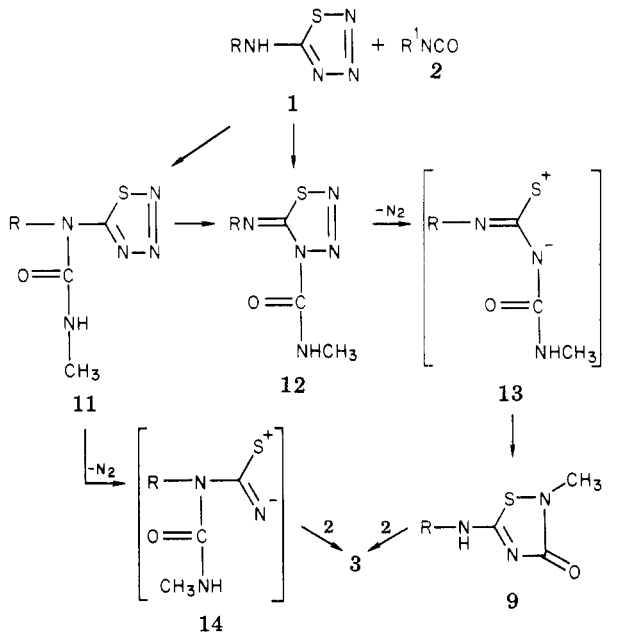
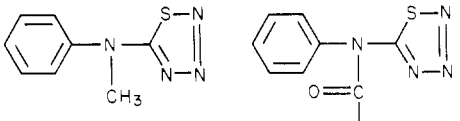
published[13] factors were used for methyl, chloro, and nitro groups. Since the substitution pattern in **4b** is the same as that for the model compounds, close agreement can be expected. The value calculated with the above factor for C_1 of the phenyl of **4b** is δ 147.3. For **3b**, the C_1 phenyl carbon downfield shift can be expected to be of much smaller magnitude, since model compounds[14] show a downfield shift of only δ 8 to 9.4 for C_1 of a phenylamino bearing two unsaturated atoms. Since **3b** shows the lowest field aromatic absorption at δ 138.3, **4b** is excluded, and **3b** is established as the correct structure. Similar calculations for **4a** give an expected value of δ 148.5, whereas the lowest field aromatic carbon absorption is found at δ 135.2.

Scheme III



Further proof for **3** is provided by the ^1H NMR of **3d**, which shows the methyl group of the 5-(methylamino) at δ 3.32,[15] whereas a 5-(methylimino) in **4d** would be expected at about δ 2.90.[16] The structure of **3c** is based on analogy to the proven structures.

The likely reaction sequences from **1** to **3** are shown in Scheme III. Some observations pertinent to this scheme follow: (1) the reaction is catalyzed by triethylamine; (2) 5-(disubstituted amino)-1,2,3,4-thiatriazoles such as **15** and **16** do not react with **2** under conditions where **1** reacts readily; and (3) reaction of equimolar amounts of **1** and **2** yields only **3** and unreacted **1**. These observations



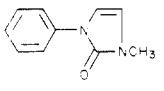
15 **16**

suggest that the slower step is the formation of **11** or **9**, the latter from **12** via the dipole **13**. The intermediate **12** can be formed directly from **1** or by rearrangement of **11**. The route through **12** appears to be more likely, since the 4-substituted thiatriazolines have been shown to add to cumulative double bonds,[5-10] but the 5-(disubstituted amino)thiatriazoles have not. The only possible exception to this general observation is a recent observation by L'abbé et al. on the reaction of **1** (R = H) with benzoyl chlorides, thiobenzoyl chlorides, and *N*-phenylbenzimidoyl chlorides.[17]

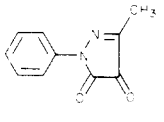
(12) G. Olah and D. J. Donovan, *J. Org. Chem.*, **43**, 860 (1978). Compounds **8**, **20**, **21**, **22**, and **23** were used for the calculations.

(13) G. C. Levy and G. L. Nelson, "Carbon-13 NMR for Organic Chemists", Wiley-Interscience, New York, 1972, p 81.

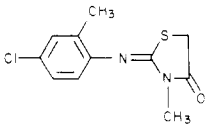
(14) M. Begtrup, *Acta Chem. Scand., Ser. B*, **28**, 61 (1974), report δ 137.9 for



and δ 136.5 for

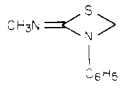


(15) A model compound



was prepared and showed *N*-methyl resonance at δ 3.32.

(16) W. Ried and O. Mösinger, *Chem. Ber.*, 111, 155 (1978), report δ 2.90 for the methyl in



Experimental Section

Melting points were determined on a Mettler FP-1 if a single value is given or on a Thomas-Hoover melting point apparatus if a range is given or if the compound decomposes. The ^{1}H NMR spectra were recorded on a Varian A-60D spectrometer and ^{13}C NMR spectra on a Varian CFT-20 spectrometer with tetramethylsilane as internal standard. Infrared spectra were recorded on a Perkin-Elmer 137 instrument.

4-(4-Chloro-2-methylphenyl)-3-thiosemicarbazide. To 27.55 g (0.150 mol) of 4-chloro-2-methylphenyl isothiocyanate[18] in 150 mL of absolute ethanol was added 7.60 g (0.150 mol) of hydrazine hydrate; the suspension was heated to reflux and diluted with ethanol until a solution was obtained. Cooling the solution to room temperature gave 26.1 g (80.7%) of 4-(4-chloro-2-methylphenyl)thiosemicarbazide, mp 159.0 °C.

Anal. Calcd for $C_8H_{10}ClN_3S$: C, 44.55; H, 4.67. Found: C, 44.24; H, 4.65.

5-[(4-Chloro-2-methylphenyl)amino]-1,2,3,4-thiatriazole (1b). The compound was prepared by the method of Lieber et al.[1] from 4-(4-chloro-2-methylphenyl)-3-thiosemicarbazide and sodium nitrite in acetic acid. Recrystallization from absolute ethanol gave **1b** in 89.5% yield. The material was slightly decomposed upon heating, and therefore the analytical sample, mp 130.5 °C dec, was obtained by dissolving the sample in ethyl acetate at room temperature and then filtering and cooling the solution to −15 °C.

Anal. Calcd for $C_8H_7ClN_4S$: C, 42.39; H, 3.11; N, 24.72. Found: C, 42.18; H, 3.03; N, 24.79.

3-Methyl-1-(2-methyl-3-oxo-Δ^4-1,2,4-thiadiazolin-5-yl)-1-phenylurea (3a). To 5.00 g (28.0 mmol) of **1a** (Aldrich Chemical Co.) in 50 mL of THF was added 5.00 mL (84.7 mmol) of methyl isocyanate and 10 drops of triethylamine. After being stirred overnight, the solution was evaporated to dryness, and the residue was recrystallized from 150 mL of absolute ethanol to yield 7.30 g (98.6%) of **3a**, mp 190.6 °C. The analytical sample, mp 192.5 °C, was obtained by recrystallization from acetonitrile: NMR ($CDCl_3$) δ 2.74 (d, 3, $NHCH_3$), 3.15 (s, 3, $SNCH_3$), 5.73 (br, 1, NH), 7.45 (m, 5, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 27.2 and 30.2 (NCH_3), 127.8, 129.0, 129.1, and 135.2 (aromatic), 152.6 (C-5), 165.4 and 166.5 (C=O); IR (Nujol) 1690 and 1608 cm^{-1}.

Anal. Calcd for $C_{11}H_{12}N_4O_2S$: C, 49.99; H, 4.58; N, 21.20. Found: C, 49.59; H, 4.65; N, 21.20.

The reaction of equimolar amounts of **1a** and **2a** under the same conditions gave only **3a** and **1a**. The detection limit by TLC (ethyl acetate, silica gel plates) for **9a** was <0.3%.

1-(4-Chloro-2-methylphenyl)-3-methyl-1-(2-methyl-3-oxo-Δ^4-1,2,4-thiadiazolin-5-yl)urea (3b). By the same procedure **3b** was obtained from **1b** and methyl isocyanate in 73.6% yield after chromatography on silica gel with 1:1 benzene–ethyl acetate. The analytical sample, mp 205.6 °C, was recrystallized from methanol: NMR ($CDCl_3$) δ 2.13 (s, 3, aryl CH_3), 2.74 (d, 3, $NHCH_3$), 3.13 (s, 3, $SNCH_3$), 5.75 (q, 1, NH), 7.0–7.4 (m, 3, aryl); ^{13}C NMR ($CDCl_3$) δ 17.5 (aryl CH_3), 27.1 and 30.2 (NCH_3), 127.1, 129.8, 131.0, 132.8, 135.2, and 138.3 (aromatic), 152.0 (C-5), 165.2 and 165.7 (C=O); IR (Nujol) 1690 and 1610 cm^{-1}.

Anal. Calcd for $C_{12}H_{13}ClN_4O_2S$: C, 46.08; H, 4.19; N, 17.91. Found: C, 45.91; H, 4.22; N, 17.85.

1-(4-Chloro-2-methylphenyl)-1-(3-oxo-2-phenyl-Δ^4-1,2,4-thiadiazolin-5-yl)-3-phenylurea (3c). By the same procedure **3c** was obtained from **1b** and phenyl isocyanate in 79.6% yield after chromatography on silica gel with 20:1 benzene–ethyl acetate. The analytical sample, mp 162.3 °C, was recrystallized from methanol: NMR ($CDCl_3$) δ 2.20 (s, 3, aryl CH_3), 7.0–7.75 (m, 16, aryl and NH); IR (Nujol) 1700, 1625, 1595 cm^{-1}.

Anal. Calcd for $C_{22}H_{17}ClN_4O_2S$: C, 60.48; H, 3.92; N, 12.82; Cl, 8.11; S, 7.34. Found: C, 60.29; H, 4.14; N, 12.90; Cl, 8.16; S, 7.34.

1,3-Dimethyl-1-(2-methyl-3-oxo-Δ^4-1,2,4-thiadiazolin-5-yl)urea (3d). By the same procedure **3d**, mp 188.0 °C, was obtained from **1c**[1] and methyl isocyanate in 74.8% yield after recrystallization from ethyl acetate: NMR ($CDCl_3$, Me_2SO-d_6) δ 2.76 (d, 3, $NHCH_3$), 3.08 (s, 3, $SNCH_3$), 3.32 (s, 3, 5-amino CH_3), 7.60 (q, 1, NH); IR (Nujol) 1710 and 1620 cm^{-1}.

Anal. Calcd for $C_6H_{10}N_4O_2S$: C, 35.63; H, 4.98; N, 27.70. Found: C, 35.89; H, 5.11; N, 27.44.

1-(4-Chloro-2-methylphenyl)-2-thiourea (5b). By a method similar to that described for 1-phenylthiourea,[19] **5b**, mp 177.0 °C, was prepared in 91.2% yield.

Anal. Calcd for $C_8H_9ClN_2S$: C, 47.88; H, 4.52; N, 13.96. Found: C, 47.86; H, 4.69; N, 13.56.

Phenylmethyl Phenylcarbamidothioate (6a). By alkylation of phenylthiourea with benzyl chloride in ethanol, followed by appropriate workup, **6a**, mp 79.4 °C (lit.[20] mp 80 °C), was obtained in 83.0% yield.

Benzyl *N*^{1}-[(Methylamino)carbonyl]-*N*-phenylcarbamidothioate (7a). To 29.1 g (0.120 mol) of **6a** in 200 mL of THF was added 7.50 mL (0.127 mol) of methyl isocyanate, the solution was stirred overnight at room temperature and refluxed for 0.5 h, the solvent was removed under reduced pressure, and the residue was recrystallized from cyclohexane–benzene to yield 32.7 g (91.1%) of **7a**, mp 102.8 °C.

Anal. Calcd for $C_{16}H_{17}N_3OS$: C, 64.19; H, 5.72; N, 14.03. Found: C, 64.62; H, 5.93; N, 13.67.

Benzyl *N*-(4-Chloro-2-methylphenyl)-*N*^{1}-[(methylamino)carbonyl]carbamidothioate (7b). To 70.2 g (0.350 mol) of **5b** in 300 mL of absolute ethanol was added 44.3 g (0.350 mol) of benzyl chloride, and the solution was refluxed for 21 h. Most of the solvent was removed under reduced pressure, the solution was diluted with water, and 29.4 g (0.350 mol) of sodium bicarbonate was added. The organic layer was taken up into benzene and washed with water and saturated salt solution and then dried over sodium sulfate and evaporated to dryness. The residue was dissolved in 250 mL of THF, and 20.0 mL (0.34 mol) of methyl isocyanate was added. The solution was stirred at room temperature for 0.5 h and then refluxed for 0.5 h. Solvent was removed under reduced pressure, and the residue was recrystallized from 1.1 L of cyclohexane and a few milliliters of benzene to yield 102.0 g (83.8%) of **7b**, mp 130.0 °C. The analytical sample, mp 130.6 °C, was obtained by recrystallizing again from cyclohexane.

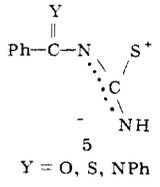
Anal. Calcd for $C_{17}H_{18}ClNOS$: C, 58.70; H, 5.22; N, 12.08. Found: C, 59.05; H, 5.33; N, 11.96.

5-Methyl-1-phenyl-2-thiobiuret (8a). To a filtered solution of 10.7 g of sodium sulfide nonahydrate in 150 mL of absolute ethanol was added 20.0 g (66.8 mmol) of **7a**, and a slow stream of hydrogen sulfide was passed through the suspension,[21] which became a solution after about 15 min, for 2 h. Nitrogen was bubbled through the solution for 2 h, the solution was poured onto ice, and the precipitate was collected and recrystallized from benzene to yield 9.50 g (68.0%) of **8a**: mp 155.0 °C; NMR (Me_2SO-d_6) δ 2.71 (d, 3, NCH_3), 6.92 (q, 1, NH), 7.15–7.8 (m, 5, aromatic), 10.11 (s, 1, NH), 12.50 (s, 1, NH).

Anal. Calcd for $C_9H_{11}N_3OS$: C, 51.66; H, 5.30; N, 20.08; S, 15.32. Found: C, 51.96; H, 5.34; N, 20.04; S, 15.11.

The same compound was also prepared by the following procedure: To 7.40 g (0.100 mol) of *N*-methylurea in 200 mL of THF was added 62.5 mL (0.100 mol) of 1.6 M *n*-butyllithium in hexane. After 0.5 h, 13.6 g (0.100 mol) of phenyl isothiocyanate was added, and the solution was refluxed for 0.5 h, cooled, and evaporated to dryness. The residue was dissolved in water and extracted with 3 × 100 mL portions of chloroform, the aqueous layer was acidified

(17) G. L'abbé, G. Verhelst, and G. Vermeulen, *Agnew. Chem., Int. Ed. Engl.*, **16**, 403 (1977). The key intermediate **5** can be formed from reaction on N-4 or the 5-amino nitrogen.



5

Y = O, S, NPh

(18) Prepared as described for α-naphthylisothiocyanate by J. Cymerman-Craig, M. Moyle, and R. A. White, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, 1963, p 700.

(19) R. L. Frank and P. V. Smith, "Organic Syntheses", Collect. Vol. III, Wiley, New York, 1955, p 735.

(20) A. E. Dixon and J. Hawthorne, *J. Chem. Soc.*, **91**, 122 (1907).

(21) S. N. Dixit, *J. Indian Chem. Soc.*, **39**, 408 (1962), describes this procedure for debenzylation of 1,5-disubstituted-2-*S*-benzyliso-4-thiobiurets.

with concentrated hydrochloric acid and extracted with ether, and the organic extracts were washed with water and saturated salt solution, dried over sodium sulfate, and evaporated to dryness. The residue was taken up in toluene, and the solution was filtered and concentrated to yield 2.85 g (13.6%) of **8a**, mp 154.4 °C. The IR and NMR spectra were identical with the spectra of **8a** prepared by the first procedure.

1-(4-Chloro-2-methylphenyl)-5-methyl-2-thiobiuret (8b). By the same procedure as that used for the preparation of **8a**, 87.0 g (0.250 mol) of **7b** yielded 50.2 g (78.0%) of **8b**: mp 177.8 °C; NMR (Me_2SO-d_6) δ 2.20 (s, 3, aryl CH_3), 2.68 (d, 3, NCH_3), 6.82 (q, 1, NH), 7.1–7.85 (m, 3, aromatic), 10.15 (s, 1, NH), 12.07 (s, 1, NH).

Anal. Calcd for $C_{10}H_{12}ClN_3OS$: C, 46.60; H, 4.69; N, 16.30. Found: C, 46.80; H, 4.73; N, 16.09.

2-Methyl-5-(phenylamino)-1,2,4-thiadiazol-3(2*H*)-one (9a).[22] To 4.18 g (20.0 mmol) of **8a** in 100 mL of absolute ethanol was added 3.20 g (20.0 mmol) of bromine while the solution was cooled in an ice bath. Ice was added immediately and the precipitate collected. Recrystallized from 1.8 L of acetonitrile gave 2.75 g (66.4%) of **9a**: mp 206.1 °C; NMR (Me_2SO-d_6) δ 3.13 (s, 3, NCH_3), 7.1–7.8 (m, 5, aromatic), 10.75 (very broad, 1, NH); IR (Nujol) 1635 cm^{-1}.

Anal. Calcd for $C_9H_9N_3OS$: C, 52.16; H, 4.38; N, 20.27. Found: C, 52.30; H, 4.42; N, 20.54.

Preparation of 3a from 9a. To 518 mg (2.50 mmol) of **9a** suspended in 20 mL of THF was added 5 drops of triethylamine and 1.00 mL (17.0 mmol) of methyl isocyanate. After 1 h, the solution was evaporated to dryness, and the residue was recrystallized from benzene to yield 475 mg (71.9%) of **3a**: mp 192.4 °C; IR and NMR spectra were identical with the spectra for **3a** prepared as described above from **1a** and methyl isocyanate.

5-[(4-Chloro-2-methylphenyl)amino]-2-methyl-1,2,4-thiadiazol-3(2*H*)-one (9b).[22] By the same procedure as that used for the preparation of **9a**, 2.91 g (11.3 mmol) of **8b** yielded 1.75 g (60.6%) of **9b**, mp 190.6 °C, after recrystallization from ethanol: NMR (Me_2SO-d_6) δ 2.26 (s, 3, aryl CH_3), 3.08 (s, 3, NCH_3), 7.15–7.9 (m, 4, aromatic and NH); IR (Nujol) 1631 cm^{-1}.

Anal. Calcd for $C_{10}H_{10}ClN_3OS$: C, 46.97; H, 3.94; N, 16.43. Found: C, 47.23; H, 3.98; N, 16.56.

(22) The oxidative cyclization of 1-substituted-2-thiobiurets by this method is described by F. Kurzer and S. A. Taylor, *J. Chem. Soc.*, 379 (1958).

Preparation of 3b from 9b. To 1.02 g (4.00 mmol) of **9b** in 20 mL of THF was added 5 drops of triethylamine and 1.00 mL (17.0 mmol) of methyl isocyanate. After 1 h, the solution was evaporated to dryness, and the residue was recrystallized from methanol to yield 0.97 g (78%) of **3b**: mp 206.4 °C; IR and NMR spectra were identical with the spectra for **3b** prepared as described above from **1b** and methyl isocyanate.

5-(*N*-Methylanilino)-1,2,3,4-thiatriazole (15). To 9.06 g (50.0 mmol) of 4-methyl-4-phenylthiosemicarbazide was added 125 mL of acetic acid, the suspension was heated to 65 °C and cooled in ice, and 3.57 g (50.7 mmol) of sodium nitrite in 15 mL of water was added at 15–18 °C. The solution was poured into 750 mL of ice–water, and the precipitate was collected, dried, and recrystallized from cyclohexane to yield 5.01 g (52.1%) of **15**, mp 56.3 °C (lit.[5] mp 56–7 °C). A second crop, mp 55.4 °C, 1.89 g (19.7%), was obtained.

Attempted Reaction of 15 with Methyl Isocyanate. To 1.92 g (10.0 mmol) of **15** in 10 mL of THF was added 5 drops of triethylamine and 1.00 mL (17.0 mmol) of methyl isocyanate. After 18 days at room temperature, the solution was evaporated. TLC (4:1 benzene–ethyl acetate) showed only **15**; the IR spectra was identical with that for **15**.

Attempted Reaction of 16 with Methyl Isocyanate. To 2.20 g (10.0 mmol) of *N*-(1,2,3,4-thiatriazol-5-yl)acetanilide (**16**)[23] in 20 mL of THF was added 0.80 mL (14 mmol) of methyl isocyanate and 5 drops of triethylamine. After 11 days at room temperature, only **16** and a trace of acetanilide could be detected by NMR spectroscopy.

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Registry No. 1a, 13078-30-3; **1b**, 71582-24-6; **1c**, 52098-72-3; **2a**, 624-83-9; **2b**, 103-71-9; **3a**, 71549-48-9; **3b**, 71549-49-0; **3c**, 71549-50-3; **3d**, 71549-51-4; **5a**, 103-85-5; **5b**, 63980-71-2; **6a**, 28269-82-1; **7a**, 71549-52-5; **7b**, 71549-53-6; **8a**, 71549-54-7; **8b**, 71549-55-8; **9a**, 71549-56-9; **9b**, 71549-57-0; **15**, 71549-58-1; **16**, 42105-60-2; 4-(4-chloro-2-methylphenyl)-3-thiosemicarbazide, 61335-37-3; 4-chloro-2-methylphenyl isothiocyanate, 23165-53-9; hydrazine hydrate, 7803-57-8; benzyl chloride, 100-44-7; 4-methyl-4-(phenylthio)semicarbazide, 21076-11-9; 2-(4-chloro-2-methylphenyl)-3-methyl-4-thiazolidone, 71549-59-2; *N*-methylurea, 598-50-5.

(23) E. Lippmann, D. Reifegerste, and E. Kleinpeter, *Z. Chem.*, **13**, 134 (1973).

Preparation and Reactions of Some Derivatives of 2,4-Benzodiazepines and 1,3-Diazepines

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Some 3-methylene- and 3-benzylidene-2,4-benzodiazepine-1,5-diones **1** and 2-methylene-1,3-diazepine-4,7-diones **2** and the related systems **4** and **5** were prepared by reacting *o*-phthaloyl chloride, succinyl chloride, furan-3,4-dicarbonyl chloride and 1-phenyl-2,5-dimethylpyrrole-3,4-dicarbonyl chloride, respectively, with *N,N'*-diarylacetamidines. 3-Phenylimino derivatives of **1** and **2** and a 3-(phenylimino)-2,4-benzodiazepin-1-one (**8**) were synthesized by treatment of *o*-phthaloyl chloride, succinyl chloride, and *o*-chloromethylbenzoyl chloride with 1,2,3-triphenylguanidine. The 3-methylene- and 3-benzylidene groups of **1** were reduced by catalytic hydrogenation to give 3-alkyl-1*H*-2,4-benzodiazepine-1,5-diones **3**. 2,3,4,5-Tetrahydro-2,4-diphenyl-3-(phenylimino)-1*H*-2,4-benzodiazepin-1-one (**8**) in polyphosphoric acid underwent a remarkable isomerization to 11-oxo-*N,N'*-diphenyl-5(6*H*)-morphanthridinecarboxamidine (**9**) in 95% yield.

Recently we communicated that treatment of *N,N'*-diphenylacetamidine with *o*-phthaloyl chloride and succinyl chloride formed the 3-methylene-2,4-benzodiazepine-1,5-dione **1a** and the 2-methylene-1,3-diazepine-4,7-dione **2a** (Scheme I).[1] Previous to our study, only one other example of a 2,4-benzodiazepinedione was known, and that a 1,3-dione.[2] We now report that the reaction of *N,N'*-diarylacetamidines with various diacyl halides is

(1) H. W. Heine and C. Tintel, *Tetrahedron Lett.*, 23 (1978).
(2) A. M. Felix and R. I. Fryer, *J. Heterocycl. Chem.*, **5**, 291 (1968).

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