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Reaction of *N*³-unsubstituted amidrazone ylides (**1a** and **1b**) with alkyl or aryl isothiocyanates gives *N*³-thiocarbamoylamidrazone ylides (**2**). Thermolysis of **2** gives 3-alkyl(or aryl)-5-alkyl(or aryl)amino-1,2,4-thiadiazoles (**3a-i**).

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In paper 4 (2) of this series, we reported that *N*³-unsubstituted amidrazone ylides (**1**) are readily obtained by the base-promoted reaction of a nitrile with 1,1,1-trimethylhydrazinium chloride (or tosylate).

In this paper, we report that alkyl or aryl isothiocyanates add to **1a** and **1b** to give excellent yields of *N*³-thiocarbamoyl substituted amidrazone ylides (**2a-i**) (3). When heated at their decomposition temperatures, **2a-i** undergo intramolecular nucleophilic attack by sulfur at *N*² to give trimethylamine and good yields of 3-alkyl(or aryl)-5-alkyl(or aryl)amino-1,2,4-thiadiazoles (**3a-i**).

We have also found that *p*-tolyl isocyanate reacts with **1a** to give the *N*³-carbamoyl substituted ylide **4**. Thermolysis of **4** afforded a complex mixture of products from which only 4,4'-dimethylcarbanilide could be isolated. In view of the unpromising results obtained from the thermolysis of **4**, we did not prepare further examples of *N*³-carbamoyl substituted ylides.

In two cases, we established that good yields of thiadiazoles (**3a** and **3c**) may be obtained by a "one-flask" procedure that does not involve isolation and purification of the intermediate ylides (**2**). Although this method was not applied to the synthesis of the other thiadiazoles in the series, it should be generally applicable.

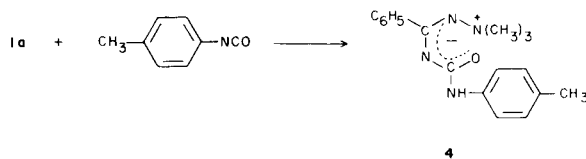
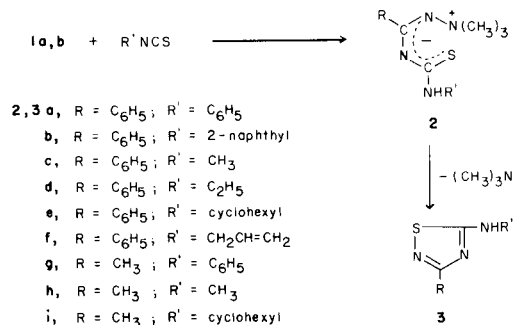
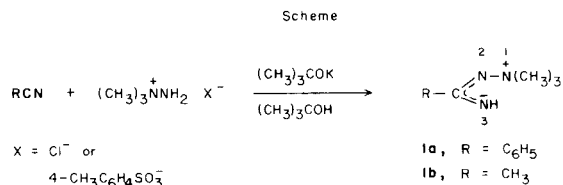
We regard our procedure as a facile method for the synthesis of the 1,2,4-thiadiazoles of type **3**. Previously employed methods for the preparation of **3** have been summarized by Kurzer and Tertiuk (4).

EXPERIMENTAL

Melting points were determined using a Mel-temp apparatus and are uncorrected. Nmr spectra were determined with a Hitachi-Perkin Elmer R24B spectrometer utilizing hexamethyldisiloxane as an internal standard. Infrared spectra were determined with a Perkin-Elmer 710B instrument. Yields are not maximized.

Preparation of *N*³-Thiocarbamoylamidrazone Ylides (**2**).

To 0.01 mole of the isothiocyanate in 20 ml. of dry benzene was added 0.01 mole of 2-(iminophenylmethyl)-1,1,1-trimethylhydrazinium hydroxide inner salt (**1a**) or 2-(1-iminoethyl)-1,1,1-trimethylhydrazinium hydroxide inner salt (**1b**). The reaction mixture was warmed on the steam bath to dissolve the added ylide. Immediate separation of the crystalline products was usually observed.



Preparation of 3-Alkyl(or aryl)-5-alkyl(or aryl)amino-1,2,4-thiadiazoles (**3**).

When heated at the decomposition temperatures given in Table I, **2a-i** underwent vigorous evolution of trimethylamine. The crude products were purified by recrystallization. With the exception of **3b**, the products have been previously reported (4,5,6) and in all cases the nmr spectra were compatible with the assigned structure. Compounds **3a** and **3c** were prepared by the published procedures and were found to be identical (nmr, ir) with the products obtained from **2a** and **2c**.

"One-Flask" Preparation of Thiadiazoles **3a** and **3c**.

Phenyl isothiocyanate (0.24 g.) was mixed with **1a** (0.31 g.). After the initial exothermic reaction had subsided, the contents of the reaction flask were heated at 210° for 5 minutes. Recrystallization of the crude product from methanol gave **3a**, 0.29 g. (66%), m.p. 168-171°.

In a similar fashion (cyclization temperature 175°), **3c** was obtained in 62% yield, m.p. 139-145°.

Table I
Analytical and Spectroscopic Data (2a-i)

| Compound No. | M.p. °C dec. | Yield (a) | Molecular Formula | Analysis | | | Ir (cm ⁻¹) | | Nmr δ (c) |
|--------------|--------------|-----------|--|------------------|----------------|------------------|------------------------|------|---|
| | | | | Calcd. | (Found) | N | NH | C=S | |
| 2a | 188-189 (d) | 77 | C ₁₇ H ₂₀ N ₄ S | 65.35 (65.16) | 6.45 (6.48) | 17.93 (17.88) | 3225 | 1240 | 3.4 (s, 9H), 7.0-7.7 (m, 10H), 9.1 (s, 1H) |
| 2b | 173-174 (d) | 100 | C ₂₁ H ₂₂ N ₄ S | 69.58 (69.36) | 6.12 (6.18) | 15.46 (15.41) | 3250 | 1230 | 3.4 (s, 9H), 7.1-7.7 (m, 12H), 9.2 (s, 1H) |
| 2c | 164-165 (e) | 61 | C ₁₂ H ₁₈ N ₄ S | 57.57 (57.61) | 7.25 (7.29) | 22.38 (22.35) | 3240 | 1230 | 2.8 [d, 3H, (s on NH → ND)], 3.4 (s, 9H), 6.9-7.5 (m, 6H, NH and aromatic) |
| 2d | 164-165 (f) | 64 | C ₁₃ H ₂₀ N ₄ S | 59.05 (59.15) | 7.63 (7.63) | 21.19 (21.14) | 3250 | 1220 | (deuteriochloroform), 1.2 (t, 3H), 3.1-3.6 [s (3.4) superimposed on m (CH ₂ CH ₃), 11H], 5.9 (bd, 1H), 7.1-7.8 (m, 5H) |
| 2e | 166-167 (f) | 50 | C ₁₇ H ₂₆ N ₄ S | 64.11 (64.24) | 8.23 (8.26) | 17.59 (17.54) | 3250 | 1220 | 0.9-2.0 (m, 10H), 3.4 (s, superimposed on m, 10H), 6.7 (bd, 1H), 7.1-7.5 (m, 5H) |
| 2f | 159-160 (f) | 65 | C ₁₄ H ₂₀ N ₄ S | 60.83 (60.78) | 7.29 (7.30) | 20.27 (20.21) | 3220 | 1230 | 3.3 (s, 9H), 3.7-4.0 (m, 2H), 4.8-5.3 (m, 2H), 6.5-6.9 (m, 1H), 6.7-7.6 (m, 6H, NH and aromatic) |
| 2g | 150-152 (e) | 83 | C ₁₂ H ₁₈ N ₄ S | 57.57 (57.63) | 7.15 (7.28) | 22.38 (22.31) | 3220 | 1230 | 2.1 (s, 3H), 3.2 (s, 9H), 6.7-7.4 (m, 5H), 9.0 (s, 1H) |
| 2h | 147-149 (f) | 87 | C ₇ H ₁₆ N ₄ S | 44.64 (44.60) | 8.57 (9.61) | 29.75 (29.67) | 3220 | 1220 | (deuteriochloroform), 2.2 (s, 3H), 2.8 (d, 3H), 3.3 (s, 9H), 6.1 (bd, 1H) |
| 2i | 153-155 (f) | 62 | C ₁₂ H ₂₄ N ₄ S | 56.20 (56.24) | 9.43 (9.46) | 21.85 (21.83) | 3240 | 1210 | (deuteriochloroform), 1.0-2.0 (m, 11H), 2.2 (s, 3H), 3.4 (s, 9H), 6.0 (bd, 1H) |

(a) Yield of crude product. (b) Potassium bromide pellets. (c) Unless otherwise specified, determined in DMSO-*d*₆. (d) Recrystallized from *N,N*-dimethylformamide. (e) Recrystallized from methanol. (f) Recrystallized from ethanol.

Table II
Properties of 1,2,4-Thiadiazoles (3a-i)

| Compound | Yield (a) | M.p. °C | Literature M.p. °C | Reference | Molecular Formula | Nmr (δ) Data (b) |
|-----------|-----------|---------|--------------------|-----------|--|---|
| 3a | 99 (c) | 164-167 | 173-174 | (4) | C ₁₄ H ₁₁ N ₃ S | 6.8-8.3 (m, 10H), 11.1 (s, 1H, exchangeable) |
| 3b | 72 | 143-145 | (d) | — | C ₁₈ H ₁₄ N ₃ S | 7.3-8.3 (m, aromatic and NH) |
| 3c | 73 | 155-157 | 155-157 | (4) | C ₉ H ₉ N ₃ S | (deuteriochloroform), 2.9 [d, 3H (s on NH → ND)], 7.2-7.6 (m, 4H, aromatic and NH), 8.0-8.4 (m, 2H) |
| 3d | 65 | 73-75 | 75 | (5) | C ₁₀ H ₁₁ N ₃ S | 1.2 (t, 3H), 3.3 [m, 2H (t on NH → ND)], 7.1-7.6 (m, 3H), 7.8-8.2 (m, 2H), 8.4 (bd, 1H, exchangeable) |
| 3e | 90 | 120-122 | 129 | (5) | C ₁₄ H ₁₇ N ₃ S | 1.1-2.1 (m, 10H), 3.4 (m, 1H), 7.2-7.5 (m, 3H), 7.9-8.2 (m, 2H), 8.4 (d, 1H, exchangeable) |
| 3f | 79 (e) | 76-78 | 82 | (6) | C ₁₁ H ₁₁ N ₃ S | 4.0 (m, 2H), 5.2 (m, 2H), 5.7-6.1 (m, 1H), 7.3-7.6 (m, 3H), 7.8-8.2 (m, 2H), 6.8 (bd, 1H, exchangeable) |
| 3g | 74 | 106-109 | 113-114 | (4) | C ₉ H ₉ N ₃ S | 2.3 (s, 3H), 6.9-7.5 (m, 5H), 10.2 (bd, 1H, exchangeable) |
| 3h | 67 | 90-92 | 96 | (5) | C ₄ H ₇ N ₃ S | (deuteriochloroform), 2.4 (s, 3H), 3.0 (s, 3H), 8.1 (bd, 1H, exchangeable) |
| 3i | 48 | 97-99 | 103 | (5) | C ₉ H ₁₅ N ₃ S | (deuteriochloroform), 0.8-2.5 [s (2.4) superimposed on m, 13H], 3.1 (m, 1H), 6.8 (bd, 1H, exchangeable) |

(a) Yield of recrystallized product. Recrystallization solvents utilized were those specified in the literature. (b) Unless otherwise specified, spectra were determined in DMSO-*d*₆. (c) Crude, unrecrystallized material that was identical (nmr, ir) with an authentic sample. (d) *Anal.* Calcd.: C, 71.26; H, 4.32; N, 13.85. Found: C, 71.09; H, 4.38; N, 13.80. (e) Recrystallized from aqueous ethanol.

Preparation and Thermolysis of 1,1,1-Trimethyl-2-[[phenyl][(4-methylphenylamino)carbonyl]amino]methylene]hydrazinium Hydroxide Inner Salt (**4**).

Addition of *p*-tolylisocyanate (1.33 g.) to **1a** (1.77 g.) resulted in an exothermic reaction. The crude solid was pulverized under 20 ml. of dry benzene. Filtration afforded **4** as a white solid, 2.1 g., m.p. 194-197° dec. Recrystallization from ethanol gave white crystals, m.p. 204-205° dec.; nmr (deuteriochloroform): δ 2.1 (s, 3H), 3.3 (s, 9H), 6.6 (s, bd, exchangeable), 6.8-7.5 (m, 9H); ir (potassium bromide): 3280 and 1620 cm^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{22}\text{N}_4\text{O}$: C, 69.65; H, 7.15; N, 18.05. Found: C, 69.75; H, 7.20; N, 17.99.

Compound **4** (1.0 g.) was heated for 15 minutes at 210°. The decomposition was accompanied by the vigorous evolution of a basic gas. Tlc of the dark red mixture (silica gel 1:20 ethanol/chloroform) revealed 8 components. Treatment of the crude mixture with 10 ml. of boiling benzene gave 80 mg. of 4,4'-dimethylcarbanilide, m.p. 253-257°, lit. m.p. 264° (7), nmr (DMSO- d_6): δ 2.2 (s, 6H), 7.0 and 7.3 (aromatic AB, 8H), 8.5 (s, 2H). The nmr spectrum of the product was identical with that obtained from an authentic sample.

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