EtOH to give an almost quantitative yield: mp 255–260 °C dec; IR 3290, 1650, 1595, 1530 cm^{-1}. Anal. Calcd for $C_{22}H_{16}N_4OS_2$: C, 63.44; H, 3.87; N, 13.45; S, 15.40. Found: C, 63.64; H, 3.81; N, 13.39; S, 15.33.

1,3-Diphenyl-5-thioxo-2,4-imidazolidinedione (5a). Treatment of **3b** in hot ethanol with an excess of concentrated HCl and dilution with water afforded **5a**: 70% yield; mp 159–162 °C (lit.[8] mp 156–158 °C).

This product can also be obtained from **4b** by the same procedure.

1,3-Diphenyl-2,5-dithioxo-4-imidazolidinone (5b). To a hot solution of 300 mg (1 mmol) of **3c** in 6 mL of 95% EtOH and 1 mL of H_2O was added 0.1 mL of 10 N HCl. The mixture was diluted with 10 mL of H_2O to give 250 mg of product (83%); mp 133–137 °C, resolidified and melted at 152–155 °C. Recrystallization from $CHCl_3$–petroleum ether provides 200 mg of product: mp 154–157 °C; IR 1731 cm^{-1}. Anal. Calcd for $C_{15}H_{10}N_2OS_2$: C, 60.38; H, 3.38; N, 9.39; S, 21.49. Found: C, 60.19; H, 3.21; N, 9.32; S, 21.25.

3-Phenyl-4-thioxo-2,5-thiazolidinedione (6). To a hot solution of 220 mg of **3c** in 5 mL of 95% EtOH was added 1 mL of 10 N HCl. A transient red color was observed. The reaction mixture was diluted with water, and the crystals were collected: yield 120 mg (72%); mp 180–183 °C. This was crystallized from $CHCl_3$–petroleum ether: mp 184–186 °C; IR 1750, 1725, 1590, 1490 cm^{-1}; ^{13}C NMR [$(CD_3)_2CO$] δ 129.2–135.3 (aromatic C), 157.1 (C-2), 183.4 (C-5), 192.8 (C-4). Anal. Calcd for $C_9H_5NO_2S_2$: C, 48.42; H, 2.26; N, 6.27; S, 28.72. Found: C, 48.14; H, 1.98; N, 6.24; S, 28.68.

Phenyldithiooxamide (7) from 3c. Through a suspension of 150 mg of **3c** in 5 mL of EtOH containing 0.07 mL of triethylamine was passed a stream of H_2S. The reaction mixture became clear and darkened slightly. Dilution with an equal volume of water gave a mixture of substances which contained mostly sulfur. Further dilution with water gave a small amount of orange needles (mp 84–86 °C), which after crystallization melted at 98–99 °C and were identical in all respects with **7** prepared from **2b** and H_2S in the presence of triethylamine (lit.[14] mp 98 °C).

1,3-Diphenyl-4-thiohydantoin (8). Through a suspension of 560 mg (2 mmol) of **3b** in 30 mL of absolute EtOH and 0.2 mL of triethylamine was passed a stream of H_2S until the system became clear. Soon thereafter a precipitate began to form. The precipitate was collected after a few minutes and washed with EtOH. The almost colorless crystals weighed 490 mg and melted at 155–175 °C. Sulfur was detected by TLC and was obtained in crystalline form from the mother liquor. Recrystallization of the product from chloroform–petroleum ether gave fine needles: mp 195–197 °C; IR 1755, 1600, 1500 cm^{-1}; ^1H NMR δ 7.0–7.7 (m, 10 H, arom), 4.75 (s, 2 H, CH_2). Anal. Calcd for $C_{15}H_{12}N_2OS$: C, 67.14; H, 4.51; N, 10.44; S, 11.95; mol wt 268.34. Found: C, 67.07; H, 4.50; N, 10.38; S, 12.22; mol wt 268, 271 (osmometric, $CHCl_3$).

4,6-Dihydro-2,4,6-triphenyl-5*H*-imidazo[4,5-*d*]thiazol-5-one (9a). To 280 mg (1 mmol) of **3b** and 110 mg (1 mmol) of benzaldehyde in 2 mL of dioxane was added 6 drops of BF_3·Me_2O. The reaction mixture warmed slightly, and the reddish precipitate of the BF_3 salt of **3b** formed rapidly. The mixture was heated under reflux for 8 h. A small amount of white, water-soluble crystals separated during this time. The reaction mixture was diluted with EtOH and filtered after being allowed to stand 1 h to give the product: 140 mg (38%); mp 154–158 °C. Recrystallization from $CHCl_3$–petroleum ether gave pale yellow crystals: mp 157–161 °C; IR 1715, 1598, and 1500 cm^{-1}; mass spectrum, m/e (relative intensity) 369 (97, M^+), 340 (51), 121 (100). Anal. Calcd for $C_{22}H_{15}N_3SO$: C, 71.52; H, 4.09; N, 11.37; S, 8.68. Found: C, 71.69; H, 3.92; N, 11.28; S, 8.75.

When **3b** was heated at 180 °C with benzaldehyde, **10a** was formed.

4,6-Dihydro-2,4,6-triphenyl-5*H*-imidazo[4,5-*d*]thiazole-5-thione (9b). When 300 mg (1 mmol) of **3c** was reacted with a twofold excess of benzaldehyde in the same way as described above, there was obtained 200 mg (61%) of **9b** (mp 262–265 °C), which after recrystallization melted at 261–263 °C: IR 1595, 1496 cm^{-1}; mass spectrum, m/e (relative intensity) 385 (97, M^+), 103 (100). Anal. Calcd for $C_{22}H_{15}N_3S_2$: C, 68.54; H, 3.92; N, 10.90; S, 16.63. Found: C, 68.47; H, 3.85; N, 10.92; S, 16.77.

The same product can be obtained in about 35% yield by heating **3c** with benzaldehyde at 180 °C for a few minutes.

5,7-Dihydro-1,3,5,7-tetraphenyldimidazo[4,5-*b*:4′,5′-*e*]pyrazine-2,6(1*H*,3*H*)-dione (10a). A mixture of 600 mg (2 mmol) of **3b** and 2 g of phenol was heated for 45 min in an oil bath at 180 °C. The reaction mixture was diluted with ethanol, and after the mixture cooled the crystals were collected: yield 160 mg (23%); mp 350–355 °C. Recrystallization from DMF gave pale yellow crystals: mp 353–355 °C; IR 1705, 1603, 1502 cm^{-1}; mass spectrum, m/e (relative intensity) 496 (100, M^+), 248 (19, M^{2+} or $M/2^+$). Anal. Calcd for $C_{30}H_{20}N_6O_2$: C, 72.57; H, 4.06; N, 16.93. Found: C, 71.92, H, 4.09; N, 16.93.

The same product was obtained by heating **3b** at 170 °C for 0.5 h.

5,7-Dihydro-1,3,5,7-tetraphenyldiimidazo[4,5-*b*:4′,5′-*e*]pyrazine-2,6(1*H*,3*H*)-dithione (10b). When **3c** was heated in phenol at 180 °C as described above, a product melting above 365 °C was obtained in 11% yield. Recrystallization from DMF gave yellow crystals which decomposed around 440 °C: IR 1595, 1498, 1422 cm^{-1}; mass spectrum, m/e (relative intensity) 528 (100, (M^+), 264 (26, M^{2+} or $M/2^+$). Anal. Calcd for $C_{30}H_{20}N_6S_2$: C, 68.16; H, 3.81; N, 15.90; S, 12.13. Found: C, 68.46; H, 3.79; N, 16.01; S, 12.16.

Registry No. 1a, 103-71-9; **1b**, 103-72-0; **2a**, 6784-22-1; **2b**, 4955-82-2; **3b**, 71342-25-1; **3c**, 74331-41-2; **4b**, 71342-37-5; **4c**, 74346-13-7; **5a**, 71342-31-9; **5b**, 74331-42-3; **6**, 74331-43-4; **7**, 17270-94-9; **8**, 74331-44-5; **9a**, 74331-45-6; **9b**, 74331-46-7; **10a**, 74331-47-8; **10b**, 74331-48-9; benzaldehyde, 100-52-7.

New Synthesis of 1,2,4-Thiadiazoles

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A new synthesis of 1,2,4-thiadiazoles has been developed. *N*′-(Thioaroyl)- (and *N*′-arylthiocarbamoyl-) *N*,*N*-dimethylamidines, which were prepared in excellent yields by reactions of thioamides (and thioureas) with *N*,*N*-dimethylalkanamide dimethyl acetals, reacted with *O*-(mesitylenesulfonyl)hydroxylamine in dichloromethane or hydroxylamine-*O*-sulfonic acid in a mixture of absolute ethanol and methanol to give 1,2,4-thiadiazoles in excellent yields.

Recently, we reported a general method[2] for the synthesis of 1,2,4-triazoles **3** and 1,2,4-oxadiazoles **4** in which the (dimethylamino)alkylidene moiety was utilized as a masked acyl function.[2-5] This method involved the re-

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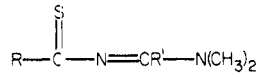
Table I. *N'*-(Thioaroyl)- (and *N'*-Arylthiocarbamoyl-) *N,N*-dimethylamidines

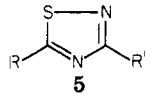


2

compd	R	R'	yield, %	mp, °C	formula[c]
2a	C_6H_5	H	97	57-59[a]	$C_{10}H_{12}N_2S$
2b	C_6H_5	CH_3	92	111-113	$C_{11}H_{14}N_2S$
2c	*p*-FC_6H_4	H	96	58-60	$C_{10}H_{11}FN_2S$
2d	3,5-$(CH_3O)_2C_6H_3$	H	97	90-92	$C_{12}H_{16}N_2O_2S$
2e	3-pyridyl	H	99	47-50	$C_9H_{11}N_3S$
2f	*p*-FC_6H_4	CH_3	90	88-90	$C_{11}H_{13}FN_2S$
2g	*p*-ClC_6H_4	CH_3	91	126-129	$C_{11}H_{13}ClN_2S$
2h	3,5-$(CH_3O)_2C_6H_3$	CH_3	92	58-60	$C_{13}H_{18}N_2O_2S$
2i	4-pyridyl	CH_3	92	95-97	$C_{10}H_{13}N_3S$
2j	C_6H_5NH	H	99	154-156[b]	$C_{10}H_{13}N_3S$
2k	*p*-FC_6H_4NH	H	94	160-161	$C_{10}H_{12}FN_3S$
2l	*m*-$CF_3C_6H_4NH$	H	95	167-169	$C_{11}H_{12}F_3N_3S$
2m	C_6H_5NH	CH_3	90	140-141	$C_{11}H_{15}N_3S$

[a] Lit.[9] mp 50-54 °C. [b] Lit.[13] no mp reported. [c] Satisfactory analytical data (±0.4% for C, H, N, S, and X, when present) were reported for all compounds in Tables I and II except those for which literature melting point values are given.

Table II. Substituted 1,2,4-Thiadiazoles

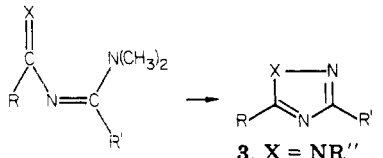


5

compd	R	R', ^{1}H-NMR, δ ($CDCl_3$)	yield, % MSH	yield, % HSA	mp, °C	formula
5a	C_6H_5	H, 8.66	87	90	26-27	$C_8H_6N_2S$
5b	C_6H_5	CH_3, 2.76	82	91	54-56[a]	$C_9H_8N_2S$
5c	*p*-FC_6H_4	H, 8.69	76	87	74-76	$C_8H_5FN_2S$
5d	3,5-$(CH_3O)_2C_6H_3$	H, 8.70	76		82-84	$C_{10}H_{10}N_2O_2S$
5e	3-pyridyl	H, 8.78		86	81-83	$C_7H_5N_3S$
5f	*p*-FC_6H_4	CH_3, 2.72	81	85	70-71	$C_9H_7FN_2S$
5g	*p*-ClC_6H_4	CH_3, 2.74	75		74-76	$C_9H_7ClN_2S$
5h	3,5-$(CH_3O)_2C_6H_3$	CH_3, 2.73	80	87	74-76	$C_{11}H_{12}N_2O_2S$
5i	4-pyridyl	CH_3, 2.79		84	70-72	$C_8H_7N_3S$
5j	C_6H_5NH	H, 8.22	75		159-161	$C_8H_7N_3S$
5k	*p*-FC_6H_4NH	H, 8.16	85		196-197	$C_8H_6FN_3S$
5l	*m*-$CF_3C_6H_4NH$	H, 8.12	79		104-106	$C_9H_6F_3N_3S$
5m	C_6H_5NH	CH_3, 2.45	79		116-118[b]	$C_9H_9N_3S$

[a] Lit. mp 50 °C,[10] 54-55.5 °C.[11] [b] Lit.[14] mp 117.5 °C.

actions of *N'*-acyl-*N,N*-dimethylamidines 1 with hydrazines (H_2NNHR'') or hydroxylamine in acetic acid to give 1,2,4-triazoles 3 or 1,2,4-oxadiazoles 4 in excellent yields.



1, X = O
2, X = S

3, X = NR''
4, X = O
5, X = S

Due to the instability of thiohydroxylamine,[6] the method could not be extended to the preparation of 1,2,4-thiadiazoles 5. The cycloaddition of the *N'*-(thioaroyl)-*N,N*-dimethylamidine 2 with ketenes or phenacyl bromides leading to the formation of 6-oxo-6*H*-1,3-thiazines or 5-acyl-2-aryl-1,3-thiazoles has been reported.[4,7] It was thus conceivable that reaction of *N'*-(thioaroyl)-*N,N*-dimethylamidines 2 with an aminating agent such as *O*-(mesitylenesulfonyl)hydroxylamine (MSH)[8] or hydroxylamine-*O*-sulfonic acid (HSA) would lead to formation of 1,2,4-thiadiazoles 5. We report here a new synthesis of 1,2,4-thiadiazoles 5 via amination–cyclization of *N'*-(thioaroyl)- (and *N'*-aroylthiocarbamoyl-) *N,N*-dimethylamidines 2.

Results and Discussion

N'-(Thioaroyl)- (and *N'*-arylthiocarbamoyl-) *N,N*-dimethylamidines 2 were prepared in 90–99% yields by reactions of thioamides (and thioureas) with *N,N*-dimethylformamide dimethyl acetal or *N,N*-dimethylacetamide dimethyl acetal (Table I). The *N'*-(thioaroyl)- (and *N'*-arylthiocarbamoyl-) *N,N*-dimethylamidines 2 then reacted with either MSH in dichloromethane at 0 °C or HSA in a mixture of absolute ethanol and methanol at room

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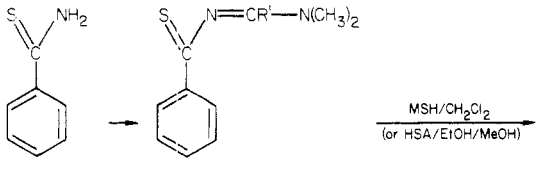
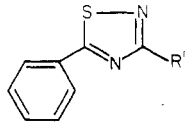
temperature to give 1,2,4-thiadiazoles **5** in 75–91% yields (Table II).

The efficiency of the new synthetic method is illustrated by the following examples. Reaction of thiobenzamide with *N,N*-dimethylformamide dimethyl acetal or *N,N*-dimethylacetamide dimethyl acetal at room temperature gave the (thiobenzoyl)formamidine **2a**[9] in 97% yield or the (thiobenzoyl)acetamidine **2b** in 92% yield. The (thiobenzoyl)formamidine **2a** then reacted with either MSH in dichloromethane at 0 °C or HSA in a mixture of absolute ethanol and methanol at room temperature to give the heretofore inaccessible 5-phenyl-1,2,4-thiadiazole (**5a**), respectively, in 87% or 90% yield. The structure as-



2a, R′ = H; 97%
2b, R′ = CH_3; 92%

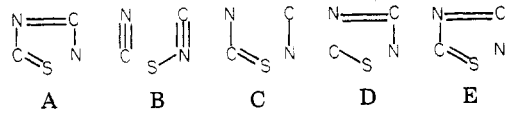


5a, R′ = H; 87% (90%)
5b, R′ = CH_3; 82% (91%)

signment of **5a** rested upon the spectral and analytical data; for example, the mass spectrum showed the molecular ion (M^+) at *m/e* 162 and the NMR spectrum in $CDCl_3$ showed three sets of signals at δ 7.3–7.6 (m, 3), 7.8–8.1 (m, 2), and 8.66 (s, 1). The (thiobenzoyl)acetamidine **2b** also reacted with MSH at 0 °C or HSA at room temperature to give 3-methyl-5-phenyl-1,2,4-thiazole (**5b**),[10,11] respectively, in 82% or 91% yield.

Eleven other 1,2,4-thiadiazoles (**5c–m**) were similarly prepared and are listed in Table II. The structures of the 1,2,4-thiadiazoles **5** synthesized in this report were all supported by NMR, IR, and elemental analysis data.

The 1,2,4-thiadiazole ring may be built up from simpler fragments in many ways, but of these only four general methods (A–D) are important. They are, respectively, illustrated by the following: (1) oxidative cyclization of *N*-(thioacyl)amidines in A;[10,12] (2) cycloaddition of nitrile sulfides to nitriles in B;[11] (3) oxidation of thioamides or thioureas in C;[12] (4) condensation of amidines with halogenated methylmercaptans or dithiocyanogen and condensation of amidoximes with arylisothiocyanates in D.[12]



A B C D E

Of these methods, only methods A and B allow preparation of 3,5 unsymmetrically disubstituted derivatives with complete regiospecificity; for example, 3-methyl-5-phenyl-1,2,4-thiadiazole (**5b**) was synthesized by method A in 70% yield[10] and by method B[11] in 6.9% yield. However, none of the above methods (A–D) allow facile preparation of 5-monosubstituted 1,2,4-thiadiazoles. Needless to say, our new amination–cyclization method (E), which provides heretofore inaccessible 5-monosubstituted 1,2,4-thiadiazoles **5a,c–e**, is a convenient and general way of constructing the 1,2,4-thiadiazole ring system.

Experimental Section

All melting points were taken on a Mel-Temp apparatus. Samples for elemental analyses were dried over phosphorus pentoxide under high vacuum for 3–24 h. IR spectra were measured on a Perkin-Elmer spectrophotometer; NMR chemical shifts (δ) are in parts per million relative to internal tetramethylsilane. Hydroxylamine-*O*-sulfonic acid was purchased from Aldrich Chemical Co.

***N*-[(Dimethylamino)methylene]thiobenzamide (2a). Typical Procedure for 2c–e.** A solution of 13.7 g (0.10 mol) of thiobenzamide in 16.0 mL (0.12 mol) of *N,N*-dimethylformamide dimethyl acetal was allowed to stand at room temperature for 1 h. The volatile materials were removed under reduced pressure without heating. Trituration of the residue with a small amount of cold ether gave 18.6 g (97%) of **2a** as reddish orange crystals: mp 57–59 °C (lit.[9] mp 50–54 °C); NMR ($CDCl_3$) δ 3.14 (s, 6 H), 7.2–7.6 (m, 3 H), 8.3–8.4 (m, 2 H), 8.66 (s, 1 H).

***N*-[1-(Dimethylamino)ethylidene]thiobenzamide (2b). Typical Procedure for 2f–i.** Thiobenzamide (30.0 g) was dissolved in 60 mL of *N,N*-dimethylacetamide dimethyl acetal (~85%) at room temperature. The reaction mixture immediately deposited 41.2 g (92%) of **2b** as orange crystals: mp 111–113 °C; NMR ($CDCl_3$) δ 2.49 (s, 3 H), 3.21 (s, 6 H), 7.2–7.6 (m, 3 H), 8.2–8.5 (m, 2 H).

Anal. Calcd for $C_{11}H_{14}N_2S$: C, 64.0; H, 6.84; N, 13.6; S. 15.5. Found: C. 64.0; H, 6.97; N, 13.7; S, 15.8.

1-[(Dimethylamino)methylene]-3-phenyl-2-thiourea (2j).[13] Typical Procedure for 2j–m. A mixture of 50.0 g of phenylthiourea and 100 mL of *N,N*-dimethylformamide dimethyl acetal was stirred at 100 °C for 1 h. At room temperature the reaction mixture deposited 67.4 g (99%) of **2j**[13] as colorless crystals: mp 154–156 °C; NMR ($CDCl_3$–Me_2SO-d_6) δ 3.08 (s, 3 H), 3.16 (s, 3 H), 6.9–8.0 (m, 5 H), 8.87 (s, 1 H), 9.04 (br s, 1 H).

Anal. Calcd for $C_{10}H_{13}N_3S$: C, 57.9; H, 6.32; N, 20.3; S, 15.5. Found: C, 58.3; H, 6.72; N, 20.3; S, 15.8.

Preparation of 1,2,4-Thiadiazoles 5. Two processes, A and B, have been developed for the synthesis of 1,2,4-thiadiazoles (**5**). Process A involved the reaction of the *N′*-(thioaroyl)- (or *N′*-arylthiocarbamoyl-) *N,N*-dimethylamidine (**2**) with *O*-(mesitylenesulfonyl)hydroxylamine (MSH) in anhydrous dichloromethane; process B involved the reaction with hydroxylamine-*O*-sulfonic acid (HSA) in a mixture of absolute ethanol and methanol. Both processes for the synthesis of 5-phenyl-1,2,4-thiadiazole (**5a**) and 3-methyl-5-phenyl-1,2,4-thiadiazole (**5b**) are described below.

5-Phenyl-1,2,4-thiadiazole (5a). Process A. To a solution of 1.92 g (0.010 mol) of **2a** in 15 mL of anhydrous dichloromethane at 0 °C was added dropwise a solution of 2.15 g (0.010 mol) of MSH in 12 mL of anhydrous dichloromethane over a period of 1–2 min. The reaction mixture was stirred at room temperature for 2 h and then diluted with 50 mL of dichloromethane. The dichloromethane solution was washed with saturated sodium bicarbonate sodium (3 × 25 mL), dried over sodium sulfate, and filtered. After removal of the dichloromethane, the residue (1.5 g) was distilled at 85 °C (0.3 mm) by a Kugelrohr apparatus to give 1.4 g (87%) of **5a** as an oil which solidified on cooling: mp 26–27 °C; NMR ($CDCl_3$) δ 7.3–7.7 (m, 3 H), 7.8–8.2 (m, 2 H), 8.66 (s, 1 H); mass spectrum, *m/e* 162 (M^+); IR (KBr) 2941, 2857, 1471, 1389, 1266, 1235, 1163, 1156, 980.4, 869.6, 763.4, 689.7, 653.6 cm^{-1}.

Anal. Calcd for $C_8H_6N_2S$ (mol wt 162.22): C, 59.2; H, 3.73; N, 17.3; S, 19.8. Found: C, 59.2; H, 3.93; N, 17.5; S, 20.1.

Process B. To a solution of 3.84 g (0.020 mol) of **2a** in a mixture of 3.2 mL (0.040 mol) of pyridine and 50 mL of absolute ethanol at room temperature was added rapidly a solution of 2.48 g (0.022 mol) of HSA in 30 mL of absolute methanol. The reaction mixture was stirred at room temperature for 1 h. The solvents were removed under reduced pressure at room temperature to

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leave a residue. The dichloromethane solution (200 mL) of the residue was washed with water (50 mL), 0.1 N NaOH solution (50 mL), and water (50 mL), dried over sodium sulfate, and filtered. After removal of the dichloromethane, the residue (3.0 g) was distilled at 86 °C (0.3 mm) by a Kugelrohr apparatus to give 2.9 g (90%) of **5a** as a colorless oil which solidified on cooling, mp 26–27 °C.

3-Methyl-5-phenyl-1,2,4-thiadiazole (5b). Process A. To a solution of 4.12 g (0.020 mol) of **2b** in 50 mL of anhydrous dichloromethane at 0 °C was added dropwise a solution of 4.30 g (0.020 mol) of MSH in 25 mL of anhydrous dichloromethane over a period of 1–2 min. The reaction mixture was stirred at room temperature for 2 h and then diluted with 80 mL of dichloromethane. The dichloromethane solution was washed with saturated sodium bicarbonate solution, decolorized with activated carbon (Darco), and filtered through a Celite pad. After removal of the dichloromethane, the residue was recrystallized from 5 mL of hexane to give 2.9 g (82%) of **5b**: mp 54–56 °C (lit. 50 °C,[10] 54–55.5 °C[11]); NMR ($CDCl_3$) δ 2.76 (s, 3 H), 7.2–7.6 (m, 3 H), 7.7–8.1 (m, 2 H); mass spectrum, *m/e* 176 (M^+) (calcd for $C_9H_8N_2S$ 176.24); IR (KBr) 1515, 1493, 1460, 1370, 1324, 1307, 1235, 1020, 934.6, 826.4, 775.2, 694.2, 673.4 cm^{-1}.

Process B. To a suspension of 4.12 g (0.020 mol) of **2b** in a mixture of 3.2 mL (0.040 mol) of pyridine and 50 mL of absolute ethanol at room temperature was added rapidly a solution of 2.48 g (0.022 mol) of HSA in 30 mL of absolute methanol. The reaction mixture was stirred at room temperature for 1 h. The solvents were removed under reduced pressure at room temperature to leave a residue. The dichloromethane solution (200 mL) of the residue was washed successively with water (50 mL), 0.1 N NaOH solution (50 mL), and water (50 mL), dried over Na_2SO_4, and filtered. After removal of the dichloromethane, the residue was recrystallized from 4 mL of hexane to give 3.21 g (91%) of **5b** as colorless crystals, mp 54–56 °C.

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Registry No. 2a, 52421-65-5; **2b**, 67229-59-8; **2c**, 74466-79-8; **2d**, 74466-80-1; **2e**, 74466-81-2; **2f**, 74466-82-3; **2g**, 74466-83-4; **2h**, 74466-84-5; **2i**, 74466-85-6; **2j**, 59819-37-3; **2k**, 74466-86-7; **2l**, 74466-87-8; **2m**, 74466-88-9; **5a**, 74466-89-0; **5b**, 50483-77-7; **5c**, 74466-90-3; **5d**, 74466-91-4; **5e**, 74466-92-5; **5f**, 74466-93-6; **5g**, 74466-94-7; **5h**, 74466-95-8; **5i**, 74466-96-9; **5j**, 74466-97-0; **5k**, 74466-98-1; **5l**, 74466-99-2; **5m**, 17467-18-4; thiobenzamide, 2227-79-4; *N,N*-dimethylformamide dimethyl acetal, 4637-24-5; *N,N*-dimethylacetamide dimethyl acetal, 18871-66-4; phenylthiourea, 103-85-5; *p*-fluorophenylthiourea, 459-05-2; *m*-(trifluoromethyl)phenylthiourea, 1736-70-5; MSH, 36016-40-7; HSA, 2950-43-8.

Some 1,3-Dipolar Cycloaddition Reactions of Nitrile *N*-Sulfides with Acetylenes and Olefins

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The generation of nitrile *N*-sulfides from iminosulfur difluorides is general. Trifluoroacetonitrile *N*-sulfide was allowed to react with some acetylenes and olefins. For example, *N*-phenylmaleimide gave *N*-phenyl-3-trifluoromethyl-1,2-thiazoline-4,5-carboximide in 74% yield.

The reaction between benzonitrile *N*-sulfide and monosubstituted electron-deficient acetylenes produced a mixture of 4- and 5-substituted isothiazoles.[1,2,7] The purpose of this research was to investigate the generality of the formation of nitrile *N*-sulfides from iminosulfur difluorides and the influence of substituents on the regiospecificity of the 1,3-dipolar cycloaddition reactions between methyl propiolate and some nitrile *N*-sulfides as well as the reactions between trifluoroacetonitrile *N*-sulfide and electron-deficient olefins.

Results and Discussion

The iminosulfur difluorides were synthesized by reacting sulfur tetrafluoride with the appropriate primary amine.[3] In the case of (benzylimino)sulfur difluoride, trimethylamine was employed as a solvent and base to react with the hydrogen fluoride produced with the formation of the iminosulfur difluoride.[4] The use of trimethylamine in the preparation of ((2,2,2-trifluoroethyl)imino)sulfur difluoride was complicated by the similarity of the boiling points of the amine and the difluoride. Since 2,2,2-trifluoroethylamine is expensive, the nonvolatile base *N,N,N',N'*-tetramethyl-1,8-diaminonaphthalene was employed. An inert solvent, having a low freezing point, because the highly exothermic reaction between amine and sulfur tetrafluoride is best conducted at −45 °C, and having a fairly high boiling point, in order to allow its convenient separation from the iminosulfur difluoride, was desirable. Toluene (fp −95 °C, bp 110 °C) was found to satisfy those requirements although it was never possible to completely remove all traces of toluene from any sample of the iminosulfur difluoride. Solutions of the iminosulfur difluoride dissolved in toluene were satisfactory for conducting the 1,3-dipolar cycloaddition reactions and therefore the need to completely remove all toluene from the iminosulfur difluoride was eliminated. (Ethylimino)sulfur difluoride was obtained by reaction of ethylamine with sulfur tetrafluoride in the absence of any solvent or other base.[5] The major disadvantage of this procedure was the formation of diethylsulfur diimide which could be easily separated from the iminosulfur difluoride by high-vacuum distillation.

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