The Chemistry of *N*-Cyanodithioimidocarbonic Acid. III. An Intermediate in Heterocyclic Synthesis

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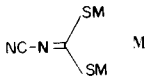
The synthesis of substituted benzimidazole, benzothiazole, oxadiazole and triazine systems from dipotassium *N*-cyanodithioimidocarbonate are described.

Scattered reports have appeared in the literature attesting to the versatility of di-alkali metal *N*-cyanodithioimidocarbonate (**1**) as an intermediate in the preparation of nitrogen- and sulfur-containing heterocycles. For example, substituted triazoles (2), imidazoles (3), and thiazoles (4-6) have been prepared from **1** in one or two steps. In each case ring formation involves nucleophilic attack on the nitrile carbon atom by a heteroatom or carbanion as illustrated in equations 1 through 3.



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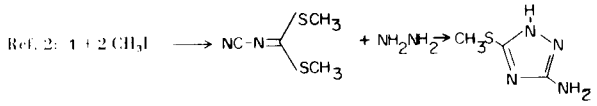

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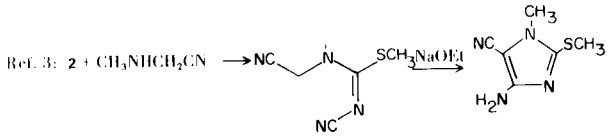
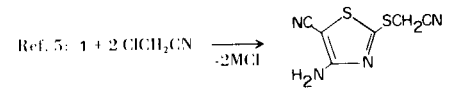
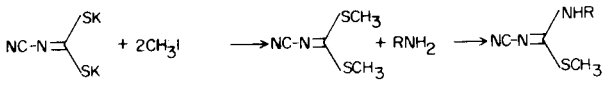




In preceeding papers (7,8) we have shown how **1** (M=K) can serve as a precursor to various 1,3-dithiolanes and 3,5-disubstituted 1,2,4-thiadiazoles as well as acyclic mono and diesters. More recently we have sought to extend the utility of **1**, a potentially low-cost compound, as a source of other heterocyclic systems along the same lines as described above. This report summarizes results obtained with intermediates **2** and **3a-d**, prepared in good yields



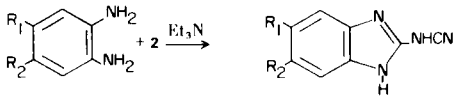
2

3a, R = H
b, R = C_6H_5
c, R = $CH(CH_3)_2$
d, R = CH_3

according to equation 4. These compounds furnish the following heterocycles in one additional step (9).

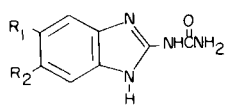
Benzimidazoles.

In the presence of triethylamine, some *o*-phenylenediamines react with **2**, to afford 2-cyanoamino benzimidazoles (**4a-c**) in fair to poor yield (eq. 5). From the cases studies, the reaction appears to be favored by electron-donating groups because yields improve with methyl substitution, but no characterizable products were obtained



4a, R_1 R_2 H
b, R_1 CH_3, R_2 H
c, R_1 R_2 CH_3

with chloro or nitro substituents. A report by D'Amico and co-workers (10) merits attention in this context because they found the reaction of *o*-phenylenediamine with **2** minus triethylamine affords 2-(methylthio)benzimidazole resulting from displacement of the elements of cyanamide rather than a second molar equivalent of methylmercaptan as required by equation 5.

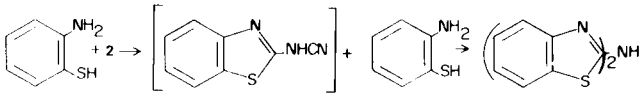


5a, R_1 R_2 H
b, R_1 CH_3, R_2 H
c, R_1 R_2 CH_3

Acid hydrolysis of the cyanoamino group of **4a-c** provided the corresponding urea derivatives **5a-c** in high yields upon workup and treatment with base.

Benzothiazoles.

In a reaction somewhat akin to the above, *o*-aminobenzenethiol with **2** afforded 2,2′ iminobis (benzothiazole), **6**, also reported by D'Amico (10) and by Neidlein and Reuter (11) (eq. 6). Preparation of **6** requires no base

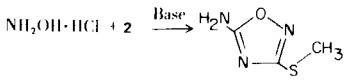


7 6

and is the major product even with non-stoichiometric quantities of the reactants. 2-Cyanoaminobenzothiazole, **7**, (12), has been proposed as an intermediate in the production of **6**, (10, 11). By controlling reaction and workup conditions, **7** can be isolated, albeit in very low yield. Subsequent treatment of **7** with a molar equivalent of *o*-aminobenzenethiol does provide **6** in high yield.

Oxadiazoles.

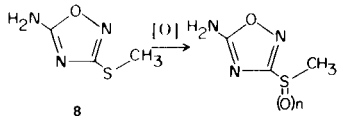
In a manner similar to hydrazine (*i.e.*, eq. 1), hydroxylamine reacted with **2** to give 5-amino-3-methyl-1,2,4-oxadiazole (**8**) as depicted in equation 7.



8

This compound is somewhat unique in that it undergoes a rapid and moderately violent decomposition at its melting point to give a white solid and a volatile component. The solid appears to be polymeric in nature and analyzes for carbon, hydrogen, nitrogen and oxygen in a ratio approximated by CH_2N_2O. The volatile component has been tentatively identified as methylthiocyanate by infrared spectrum suggesting ring cleavage at the O-N and C-N bonds.

Further reactions with **8** were generally unsuccessful because of the thermal instability, manifesting itself even below the melting point at a slower rate. However, oxidation of the subsitituent methylthio sulfur atom in **8** with one and two molar equivalents of *m*-chloroperbenzoic acid under mild conditions did afford the corresponding sulfoxide **8a** and sulfone **8b**, respectively (eq. 8). Based on qualitative observations, the sulfoxide displays thermal instability to a lesser extent than **8** and the sulfone, not at all.



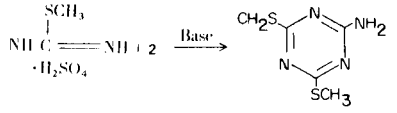
8 8a, n 1
b, n 2

Triazines.

Three routes to substituted 1,3,5-triazines via either **2** or **3** have been uncovered and these are dealt with separately.

Reaction of **2** with *S*-Methylisothiourea.

In a straightforward manner analogous to previously described reactions, *S*-methylisothiourea with **2** afforded 2-amino-4,6-dimethylthio-1,3-5-triazine, **9**, in 61% yield (eq. 9). This compound was first reported by A. Hofmann in 1885 (13) from 2,4,6-trimethylthio-1,3,5-triazine and alcoholic ammonia.



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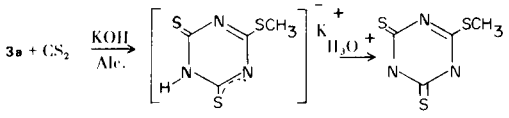
Reaction of **3** with Carbon Disulfide or Hexafluoroacetone.

Taylor, *et al.*, have published a number of papers dealing with the utilization of *o*-aminonitriles in heterocyclic synthesis (14). *N*-Substituted *N*′-cyano-*S*-methylisothioureas, of which **3a-d** are representative, can be considered hetero equivalents of the *o*-aminonitriles studied by Taylor, and therefore might be expected to undergo comparative transformations. This approach has been realized in the cases of carbon disulfide and hexafluoroacetone.

Reaction of **3a** with carbon disulfide in methanolic potassium hydroxide (Triethylamine in chloroform gave no reaction.) resulted in production of a monopotassium salt assigned structure **10** (eq. 10).

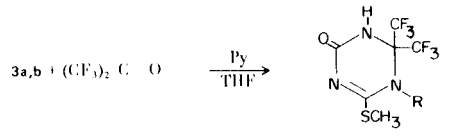


10 11

The transformation of **3a** to **10** probably involves a thiadiazine intermediate that irreversibly rearranges to **10** in the presence of base (14). Acidification of **10** provided **11**, and mono- and dialkylation of **10** with one or two molar equivalents of methyl iodide under neutral conditions afforded the dimethyl **12** and trimethyl **13** (15) homologues, respectively.

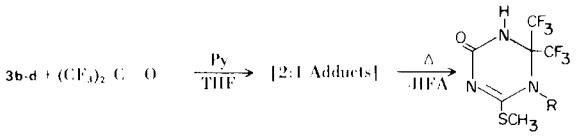
α-Fluoroketones, of which hexafluoroacetone (HFA) is a prime example, are chemically atypical of most aliphatic ketones because of the considerable carbonyl charge polarization induced by the α-fluorine atoms. Thus, hexafluoroacetone undergoes a variety of interesting reactions with compounds reminescent of **3** to give new heterocycles (16-18). When **3a** and **3b** were reacted with stoichiometric amounts of hexafluoroacetone in the pres-

ence of pyridine under anhydrous conditions, substituted 1,3,5-triazinones **14a** and **14b** were isolated in high yields (eq. 11). By anology with a previously suggested mechan-



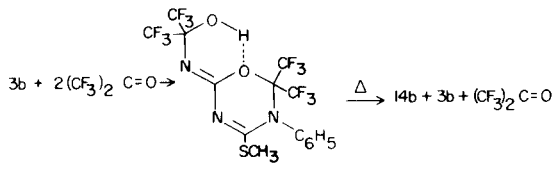
14a, R H
b R C_6H_5

ism (18), formation of **14a** and **14b** is viewed as a series of equilibrium steps culminating in an irreversible Chapman-type rearrangement to give the indicated products. With an excess of hexafluoroacetone, reaction of **3b-d** afforded different compounds believed to be 2:1 adducts of hexafluoroacetone and **3b-d**. Pyrolysis of these adducts provided the 1,3,5-triazinones **14b-d** (eq. 12). Although the



14b, R C_6H_5
c, R $CH(CH_3)_2$
d, R CH_3

adducts from **3c** and **3d** were unstable liquids, **3b** gave a low melting solid which could be purified by recrystallization. This compound, **15**, analyzed correctly for 2HFA:**3b**. Pyrolysis of pure **15** at 130° afforded **14b** (contaminated with **3b**) and slightly more than one molar equivalent of hexafluoroacetone. The production of **3b** in the pyrolysis of **15** suggests that **15** may be an oxadiazine trapped by excess hexafluoroacetone prior to rearrangement as shown in equation 13. This explanation is supported by the fact that **14b** is thermally stable well above 130°. Furthermore, **15** could conceivably yield **3b** by loss of two molar equivalents of hexafluoroacetone or



15

14b by loss of one molar equivalent of hexafluoroacetone followed by rearrangement. The latter course appears to be heavily favored judging from the experimental results.

EXPERIMENTAL

Melting points were determined in open capillary tubes with a Thomas-Hoover melting point apparatus and are uncorrected. Ir and nmr spectra were recorded on a Perkin-Elmer Model 621 grating spectrophotometer and Varian Model T-60, respectively. Mass spectra were obtained through the services of Morgan-Schaffer Corp., Montreal, Conada. Microanalyses were performed by the Scott Analytical Department.

Dipotassium *N*-Cyanodithioimidocarbonate (**1**) and Dimethyl *N*-Cyanodithioimidocarbonate (**2**).

The dipotassium salt, **1**, was prepared from cyanamide and carbon disulfide in the presence of two molar equivalents of potassium hydroxide (ethanol solvent) in 85-90% yield (8). Alkylation of **1** with two molar equivalents of methyl iodide in acetone provided **2** in comparable yields (7).

N-Substituted *N'*-Cyano-*S*-Methylisothioureas, **3a-d**.

All of these compounds have been reported (19, 20) and were prepared in the same manner as described from **2** and ammonia or the appropriately substituted amines in an alcohol solvent; isopropanol was generally preferred. The structures of these compounds were verified from spectral data and melting point comparisons.

Example Procedure for Preparing Benzimidazole Cyanamides 2-Cyanoaminobenzimidazole (**4a**).

Dimethyl *N*-cyanodithioimidocarbonate (**2**), 14.6 g. (0.10 mole), *o*-phenylenediamine, 10.8 g. (0.10 mole), and 6 ml. of triethylamine were refluxed in 100 ml. of anhydrous ethanol (nitrogen atmosphere) for 2 hours. Reflux periods for the other compounds varied from 2 to 4 hours. Yields did not appear to improve with longer reflux times. Removal of the solvent *in vacuo* gave a dark brown residue that was triturated with acetone. The acetone insoluble portion was filtered, washed several times with acetone and dried to give 6.4 g. (41% of theoretical) of crude 2-cyanoaminobenzimidazole, m.p. 215-225° dec. Evaporation of the acetone-soluble portion gave a black, tarry liquid that was not investigated further. Similar intractable residues were obtained in the other cases. Recrystallization of crude product from ethanol-water afforded pure **4a** as small, colorless needles, m.p. 240° (shrinks), 258-264° (fuses), 275-285° dec., (lit., (21), 240°, 250-260° dec); ir (potassium bromide): 2169 cm^{-1} (C≡N); nmr (DMSO-d_6) δ 7.18 (4, s, C_6H_4-), 12.25 (2, s, exchange with deuterium oxide, 2-N*H*).

Anal. Calcd. for $C_8H_6N_4$: C, 60.75; H, 3.82; N, 35.42. Found: C, 60.55, H, 3.94; N, 35.46.

2-Cyanoamino-5-methylbenzimidazole (**4b**).

Compound **4b** was obtained in 50% yield. Recrystallization of the crude product from ethanol-water afforded pure **4b** as small needles, m.p. > 300°, ir (potassium bromide): 2203 cm^{-1} (C≡N); nmr (DMSO-d_6, TMS) δ: 2.35 (3, s, CH_3), 7.01 (3, m, phenyl protons), 12.14 (2, broad s, exchange with deuterium oxide, 2-N*H*).

Anal. Calcd. for $C_9H_8N_4$: C, 62.78; H, 4.68; N, 32.54. Found: C, 62.82; H, 4.82; N, 32.31.

2-Cyanoamino-5,6-dimethylbenzimidazole (**4c**).

This compound was obtained in 65% yield and recrystallized from ethanol-water; amorphous yellow solid, m.p. > 300°, ir (potassium bromide): 2141 cm^{-1} (C≡N); nmr (DMSO-d_6, TMS) δ 2.24 (6, s, 2-CH_3), 6.96 (2, s, phenyl protons), 11.99 (2, broad s, exchange with D_2O, 2-N*H*).

Anal. Calcd. for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41; N, 30.09. Found: C, 64.48; H, 5.47; N, 30.32.

2-Ureidobenzimidazole (**5a**).

2-Cyanoaminobenzimidazole (**4a**), 6.3 g. (40 mmoles) was covered with 20 ml. concentrated hydrochloric acid and the mixture heated on a steam bath for approximately five minutes. At first a clear solution was obtained, but a precipitate formed shortly thereafter. The reaction mixture was diluted with 50 ml. water, cooled to 5°, and the insoluble solid removed by filtration. Further workup afforded 7.4 g. (87% of theoretical) of the hydrochloride salt. This was dissolved in 200 ml. of water and 10% aqueous sodium hydroxide added to precipitate the free base. Recrystallization of crude product from ethanol-water gave pure **5a** as white needles, m.p. >300° (lit., (21) >300°); ir (potassium bromide) 1695 cm^{-1} (C=O), 3300 cm^{-1} (NH); nmr (DMSO-d_6, TMS) δ: 6.85 (2, s, exchange with deuterium oxide, 2-N*H*).

5-Methyl-2-ureidobenzimidazole (**5b**).

2-Cyanoamino-5-methylbenzimdazole (**4b**), 6.0 g. (35 mmoles), was stirred and refluxed for 1.5 hours in 60 ml. of 6*N* hydrochloric acid. When cooled, the insoluble hydrochloride salt was removed by filtration and dried to give 7.1 g. (90% of theoretical). The free base was obtained by dissolving the salt in hot water and neutralizing with 10% aqueous sodium hydroxide solution. Recrystallization of the grey precipitate from ethanol-water gave pure **5b** as a white granular solid, m.p. >300°; ir (potassium bromide): 1700 cm^{-1} (C=O), 3380 cm^{-1} (NH); nmr (DMSO-d_6, TMS) δ: 2.34 (3, s, C*H*$_3$), 6.80 (2, s, exchange with deuterium oxide, N*H*$_2$), 6.85 (1, d (J = 9Hz), C_6-*H*), 7.20 (1, broad s, C_4-*H*), 7.25 (1, d (J = 9 Hz), C_7-*H*), 10.50 (2, broad s, exchange with deuterium oxide, 2-N*H*).

Anal. Calcd. for $C_9H_{10}N_4O$: C, 56.83; H, 5.30; N, 29.46. Found: C, 56.85; H, 5.76; N, 29.58.

5,6-Dimethyl-2-ureidobenzimidazole (**5c**).

In the same manner as described for **5b**, 5.3 g. of hydrochloride salt (78% of theoretical) was obtained. Recrystallization of the free base from ethanol gave pure **5c** as small, white needles, m.p. >300° (sublimes); ir (potassium bromide), 1710 cm^{-1} (C=O), 3400-2850 cm^{-1} (NH); nmr (DMSO, TMS) δ: 2.25 (6, s, C*H*$_3$), 6.85 (2, s, exchange with deuterium oxide, N*H*$_2$), 7.19 (2, s, phenyl protons), 10.14 (2, s, exchange with deuterium oxide, 2-N*H*).

Anal. Calcd. for $C_{10}H_{12}N_4O$: C, 58.81; H, 5.92; N, 27.43. Found: C, 58.95; H, 5.78; N, 27.47.

2-Cyanoaminobenzothiazole (**7**).

A solution of dimethyl *N*-cyanoimidodithiocarbonate (**2**), 7.3 g. (50 mmoles), and *o*-aminobenzenethiol, 6.3 g. (50 mmoles), in 100 ml. of anhydrous ethanol (nitrogen atmosphere) was refluxed for 1 hour. When cooled, the insoluble white solid was removed by filtration, washed with ether and dried to give 3.8 g. of 2,2′-iminobis(benzothiazole), m.p. 254-256° (lit (10, 11) 262-263° and 257-258°). Evaporation of the filtrate *in vacuo* afforded a yellow semi-solid material that was triturated with an ether-hexane solution. This treatment afforded 5.2 g. of solid, m.p. 135-148°, which was dissolved in hot ethyl acetate. When cooled, 1.4 g. of solid, m.p. 175-177°, crystallized. Recrystallization from ethyl acetate gave 200 mg. of pure **7** as colorless platelets, m.p. 181-182° (lit (12) 181°); ir (potassium bromide): 2169 cm^{-1} (C≡N); nmr (DMSO-d_6, TMS) δ: 7.36 (4, m, phenyl protons), *ca.* 12.50 (1, very broad, exchanges with deuterium oxide, N*H*). Mass: *m/e* 175, M + (mw=175).

Anal. Calcd. for $C_8H_5N_3S$: C, 54.84; H, 2.88; N, 23.98. Found: C, 54.82; H, 3.29; N, 23.70.

Conversion of **7** to **6**.

2-Cyanoaminobenzothiazole (**7**), as obtained above, 1.1 g. (6.3 mmoles), and *o*-aminobenzenethiol, 0.8 g. (6.3 mmoles), was refluxed for 1 hour in 30 ml. of anhydrous ethanol (nitrogen atmosphere). The odor of ammonia was evident during the reflux period. Workup of the reaction mixture afforded 1.4 g. (83% of theoretical) of product which compared in all respects with **6** previously obtained.

5-Amino-3-methylthio-1,2,4-oxadiazole (**8**).

To a stirred slurry of dimethyl *N*-cyanodithioimidocarbonate (**2**), 9.5 g. (65 mmoles), and hydroxylaminehydrochloride, 6.6 g. (95 mmoles), in 50 ml. of water at 35° was added dropwise over a period of 1 hour sodium hydroxide, 3.8 g. (95 mmoles), in 50 ml. water. During the base addition, a colorless, gummy solid formed on the sides of the reaction vessel. Upon completion of the addition, the reaction mixture was vigorously stirred for 2 hours at ambient temperature. Extraction of the mixture with ether and workup of the ether soluble portion afforded a white solid. This was slurried in petroleum ether (30-60°), filtered and air dried to give 6.8 g. (80% of theoretical) of crude **8**, m.p. 97-99° dec. Recrystallization from ether-pentane gave pure **8** as colorless prisms, m.p. 102-103° dec.; ir (potassium bromide): 3268-3086 cm^{-1} (oxadiazole ring). Nmr (deuterioacetonitrile, TMS) δ: 2.50 (3, s, SC*H*$_3$), 6.28 (2, broad s, exchange with deuterium oxide, N*H*$_2$); mass: *m/e* 131, M + (mw=131).

Anal. Calcd. for $C_3H_5N_3OS$: C, 27.47; H, 3.84; N, 32.04. Found: C, 27.28; H, 3.92; N, 32.47.

Decomposition Products from **8**.

A freshly recrystallized sample of **8**, 1.0 g. (8 mmoles) was placed in 15 ml. of chlorobenzene and the mixture was heated on a steam bath for 1 hour. The material melted and slowly disintegrated with evolution of a gas. Chlorobenzene was removed by decantation and the white, gummy residue triturated with 95% ethanol to separate 140 mg. of white powder, m.p. >300°; ir (potassium bromide): 3400-3000 cm^{-1} (broad, essentially featureless bands), 2190 cm^{-1} (relatively sharp band, C≡N), 1750-1400 cm^{-1} (also braod, essentially featureless bands).

Anal. (Unknown solid) Found: C, 27.15; H, 4.14; N, 44.91. With oxygen as the remaining element (23.80%), these values correspond to $CH_{1.8}N_{1.4}O_{0.6}$.

In another experiment, freshly recrystallized **8**, 150 mg. was placed in a tube and immersed in an oil bath at 100°. Rapid decomposition ensued and the vapor was collected immediately in an evacuated 10 cm. gas infrared cell. The ir spectrum, although weak, exhibited bands in the same regions as methyl thiocyanate (Sadtler #20002). An ir spectrum of the white solid residue closely resembled the unknown product obtained in the previous experiment.

5-Amino-3-methylsulfinyl-1,2,4-oxadiazole (**8a**).

To a stirred slurry of 5-amino-3-methylthio 1,2,4-oxadiazole (**8**), 5.9 g. (45 mmoles), in 50 ml. of ether previously cooled to 5° was added dropwise over a period of 1 hour *m*-chloroperbenzoic acid, 8.6 g. (50 mmoles), dissolved in 100 ml. of ether. Upon completion of the addition, the reaction mixture was stirred for 1 hour at 5° and overnight at ambient temperature. The product was removed by filtration, 4.3 g. (65% of theoretical), m.p. 114-118° dec. Recrystallization from ethyl acetate afforded pure **8a** as a white, granular solid m.p. 107.5-109.5° dec.; ir (potassium bromide): 3250, 3175, 1671 cm^{-1} (NH), 1492, 1291 cm^{-1} (oxadiazole ring), 1034 cm^{-1} (S → O); nmr (deuterioacetonitrile, TMS) δ: 2.98 (3, s, S(O) C*H*$_3$), 6.60 (2, broad s, exchange with deuterium, N*H*$_2$).

Anal. Calcd. for $C_3H_5N_3O_2S$: C, 24.49; H, 3.42; S, 21.79. Found: C, 24.51; H, 3.51; S, 21.61.

5-Amino-3-methylsulfonyl-1,2,4-oxadiazole (**8b**).

In the same manner as described above, **8** was reacted with two molar equivalents of *m*-chloroperbenzoic acie to give 7.3 g. (75% of theoretical) of crude **8b**, m.p. 115-125° (contaminated with sulfoxide). Recrystallization from water afforded pure 5-amino-3-methylsulfonyl-1,2,4-oxadiazole as colorless prisms, m.p. 135-136.5°; ir (potassium bromide): 3398, 3250, 3175 cm^{-1} (NH), 1325, 1152 cm^{-1}(SO_2), 1574, 1500 cm^{-1} (oxadiazole ring); nmr (DMSO-d_6, TMS) δ: (s, 3, SO_2CH_3), 8.55 (s, 2, NH_2).

Anal. Calcd. for $C_3H_5N_3O_3S$: C, 22.08; H, 3.09; N, 25.76. Found: C, 22.20; H, 3.08; N, 26.05.

2-Amino-4,6-di(methylthio)-1,3,5-triazine (**9**).

To a stirred slurry of dimethyl *N*-cyanodithioimidocarbonate (**2**), 14.6 g. (0.1 mole), and *S*-methylisothiourea sulfate, 27.8 g. (0.1 mole), in 100 ml. of water at 40° was added dropwise over a period of 1 hour potassium hydroxide, 11.5 g. (0.2 mole), in 50 ml. of water. A gummy white solid percipitated during the base addition. Upon completion of the addition, the reaction mixture was vigorously stirred for 2 hours at ambient temperature. Workup gave 11.4 g. (61% of theoretical) of crude **9**, m.p. 197-199°. Recrystallization from ethanol-water afforded pure **9** as colorless leaflets, m.p. 200-201°(lit (13) 200°); ir (potassium bromide): 3344, 3236 cm^{-1}(NH), nmr (DMSO-d_6, TMS) δ: 2.43 (6, s, SCH_3), 7.39 (2, s, exchange with deuterium oxide, $-NH_2$).

Anal. Calcd. for $C_5H_8N_4S_2$: C, 31.90; H, 4.28; N, 29.76. Found: C, 32.20; H, 4.44; N, 29.53.

2-Methylthio-1,3,5-triazin-4,6(3*H*,5*H*)-dithione (**11**) and Monopotassium Salt (**10**).

To a stirred slurry of *N*-cyano-*S*-methyl isothiourea (**3a**), 18.0 g. (0.16 mole), and carbon disulfide, 15.2 g. (0.20 mole), in 175 ml. of 95% ethanol at 45° was added dropwise over a period of 1 hour potassium hydroxide, 9.3 g. (0.16 mole) in 75 ml. of 95% ethanol. A clear yellow solution formed during the addition. The reaction mixture was warmed to 60° and stirred for 24 hours. The insoluble crystalline solid was removed by filtration, washed with ether and dried to give 10.3 g. (29% of theoretical) of crude **10**. Recrystallization from ethanol-water afforded pure **10** as colorless prisms, m.p. $> 300°$; ir (potassium bromide): 3072, 2900 (NH), 1525, 1435, 1217, 1180 (sh), 1166, 869, 855 cm^{-1}; nmr (deuterium oxide, DDS) δ: 2.56 (3, s, $-SCH_3$), 4.67 (*H*OD).

Anal. Calcd. for $C_4H_4N_3S_3K$: C, 20.94; H, 1.76; N, 18.32; K, 17.04. Found: C, 21.30; H, 2.00; N, 18.45; K, 17.05.

Treatment of an aqueous solution of **10**, 7.0 g., with hydrochloric acid precipitated 5.5 g. of **11** as a yellow solid. Recrystallization of **11** from dimethylformamide-water gave pure material as yellow rods, m.p. $> 300°$ (sublimes); ir (potassium bromide): 3020, 2890 (NH), 1565, 1515, 1260 (sh), 1243, 1155, 1036 (sh), 872, 852 cm^{-1}; nmr (DMSO-d_6, TMS) δ: 2.50 (3, s, SCH_3), 10.34 (1, broad s, exchanges with deuterium oxide, N*H*), 15.21 (1, broad s, exchanges with deuterium oxide, N*H*); Mass: *m/e* 191, M + (mw=191).

Anal. Calcd. for $C_4H_5N_3S_3$: C, 25.11; H, 2.63; N, 21.98. Found: C, 24.97; H, 3.09; N, 22.04.

2,4-Dimethylthio-1,3,5-triazin-6(5*H*)thione (**12**).

To **10**, 1.7 g. (7 mmoles), in 35 ml. of water was added methyl iodide, 1.4 g. (10 mmoles), in one portion. The reaction mixture was stirred for 1 hour at ambient temperature. The insoluble portion was filtered, washed with water and dried to give 1.3 g. (90% of theoretical) of crude **12**, m.p. 189-193° dec. Tlc showed the product was contaminated with a trace of fully methylated **13**. Recrystallization from 95% ethanol gave pure **12** as colorless prisms (slight yellow cast), m.p. 208-210° (sublimes); ir (potassium bromide): 3075, 2870, 2700 (NH), 1535, 1495, 1230, 1190, 1130, 850, cm^{-1}; nmr (DMSO-d_6, TMS) δ: 2.54 (6, s, SCH_3), approximately 9.25 (1, very broad peak, exchanges with deuterium oxide, N*H*).

Anal. Calcd. for $C_5H_7N_3S_3$: C, 29.25; H, 3.44; S, 46.85. Found: C, 29.15; H, 3.89; S, 46.57.

2,4,6-Trimethylthio-1,3-5-triazine (**13**).

To **10**, 4.0 g. (18 mmoles), in 75 ml. of acetone and 10 ml. of water was added dropwise methyl iodide, 5.0 g. (35 mmoles), in 25 ml. of acetone. The reaction mixture was refluxed for 1 hour, cooled and the insoluble solid filtered, washed with acetone and dried affording 2.5 g. (70% of theoretical) of crude **13**, m.p. 185-186°. Pure **13** was obtained by recrystallizing from acetone to give colorless needles, m.p. 187-188° (lit (15) 188°); nmr (deuterioacetone, TMS) δ: 2.59 (s, SCH_3).

2,2-bis(Trifluoromethyl)-4-methylthio-1,3,5-triazin-6(1*H*,3*H*)one (**14a**).

Hexafluoroacetone, 9.0 g. (5.4 mmoles), was introduced below the surface of a slurry of **3a**, 5.8 g. (50 mmoles) in 100 ml. of anhydrous THF and 10 drops of pyridine at ambient temperature (slightly exothermic). The reaction mixture was stirred for 4 hours at 35-40°. Removal of the solvent *in vacuo* gave a white semi-solid which was triturated with pentane to obtain upon further workup 11.9 g. (84% of theoretical) of crude **14a**, m.p. 142-144° dec.; recrystallization from benzene-hexane gave pure **14a**, m.p. 147-148° dec.; ir (potassium bromide): 1680 cm^{-1} (C=O), 3350, 3100 cm^{-1} (NH), 1300-1155 cm^{-1} (CF_3); nmr (deuteriochloroform, TMS) δ: 2.31 (3, s, SCH_3), 7.55 (2, broad s, exchange with deuterium oxide, 2-N*H*); Mass *m/e* 281, M + (mw=281).

Anal. Calcd. for $C_6H_5F_6N_3OS$: C, 25.63; H, 1.79; N, 14.94; S, 11.40. Found: C, 25.85; H, 1.81; N, 14.99; S, 11.16.

N^3-Phenyl-2,2-bis(trifluoromethyl)-4-methylthio-1,3,5-triazin-6-(1*H*)one (**14b**).

In the same manner as described for **14a**, the reaction of hexafluoroacetone, 6.1 g. (37 mmoles), and **3b**, 6.9 g. (36 mmoles), afforded 11.6 g. (90% of theoretical) of crude **14b** as a white solid, m.p. 198-211°. This was recrystallized from chlorobenzene to prodive pure **14b** as colorless prisms, m.p. 213.5-214.5°; ir (potassium bromide): 1693 cm^{-1} (C=O), 3185, 3090, cm^{-1} (NH), 1290-1210 cm^{-1} (CF_3); nmr (DMSO-d_6, TMS) δ: 2.31 (3, s, SCH_3), 7.58 (5, m, phenyl protons), no N*H* evident, but addition of deuterium oxide resulted in an HOD peak.

Anal. Calcd. for $C_{12}H_6F_6N_3OS$: C, 40.34; H, 2.54; F, 31.90; N, 11.76; S, 8.97. Found: C, 40.52; H, 3.00; F, 32.24; N, 11.35; S, 9.17.

When the above experiment was repeated with an undetermined excess of hexafluoroacetone introduced as a gas into the reaction mixture, a low melting solid (**15**) was obtained upon workup. Recrystallization of **15** from pentane yielded a white crystalline solid, m.p. 69-71° dec.; ir (potassium bromide): 1610, 1568 cm^{-1} (C=N), 1273-1180 cm^{-1} (CF_3); nmr (deuteriochloroform, TMS) δ: 2.50 (3, s, SCH_3), 7.40 (5, m, phenyl protons), 11.60 (1, s, exchanges with deuterium oxide, -O*H*).

Anal. Calcd. for $C_{15}H_9F_{12}N_3O_2S$: C, 34.43; H, 1.73; N,

8.03; S, 6.13. Found: C, 34.55; H, 2.16; N, 8.23; S, 6.29.

A 5.0 g. sample of the 2:1 (hexafluoroacetone-**3b**) adduct (15) was pyrolyzed at 130°. There was recovered 3.2 g. of **14b** contaminated with about 10% of **3b** judging from spectral and tlc data. The calculated weight loss for one molar equivalent of hexafluoroacetone is 1.79 g.; found: 1.80 g.

In the preparation of the next two compounds, **14c** and **14b**, with an excess of hexafluoroacetone, liquid materials were obtained. Pyrolysis of these gave the desired compounds indicating adducts were also formed initially.

N^3-Isopropyl-2,2-bis(trifluoromethyl)-4-methylthio-1,3,5-triazin-6-(1*H*)-one (**14c**).

To a stirred solution of **3c**, 7.7 g. (49 mmoles) in 150 ml. of anhydrous acetonitrile (alternate solvent for these reactions) containing 5 drops of pyridine was added a stream of hexafluoroacetone below the solvent until heat evolution subsided. The reaction mixture was diluted with a slightly acidic aqueous solution and extracted with ether. Volatile components were removed from the organic portion to give 22.7 g. (95% of theoretical based on a 2:1 adduct) of colorless liquid. Pyrolysis of this at 65° and recrystallization of the resulting solid from ligroin provided 10.0 g. of pure **14c**, m.p. 117-119°; ir (potassium bromide): 1712 cm^{-1} (C=O), 3190, 3090 cm^{-1} (NH), 1300-1200 cm^{-1} (CF_3); nmr (DMSO-d_6, TMS) δ: 1.45 (6, d (J = 6 Hz), ($CH(CH_3)_2$), 2.42 (3, s, SCH_3), 4.32 (1, m (J = 6 Hz), $CH(CH_3)_2$), 7.59 (1, broad s, exchanges with deuterium oxide, N*H*).

Anal. Calcd. for $C_9H_{11}F_6N_3OS$: C, 33.44; H, 3.43; N, 13.00; S, 9.92. Found: C, 33.29; H, 3.78; N, 12.80; S, 9.42.

N^3-Methyl-2,2-bis(trifloromethyl)-4-methylthio-1,3,5-triazin-6-(1*H*)one (**14d**).

To a vigorously stirred slurry of **3d**, 77.4 g. (0.6 mole), in 500 ml. of anhydrous tetrahydrofuran containing 5 ml. of pyridine was added hexafluoroacetone through a gas addition tube until heat evolution subsided and a clear solution was obtained; then about 15 minutes longer (total addition time = 2.5 hours). When cooled, solvent was removed from the reaction mixture *in vacuo* to yield approximately 270 g. of viscous oil. This was dissolved in benzene-hexane and cooled. A solid crystallized that, upon further workup, was found to weigh 29.6 g.; identified later as **14d**. Evaporation of the filtrate from above gave 219 g. of a semi-solid material which resembled the ir spectrum of the adduct obtained from preparing **14b**. Pyrolysis of this at 80-90° yielded crude **14d** which was recrystallized from benzene-hexane to give a total of 119.4 g. (87% of theoretical with previous 29.6 g.), of pure **14d** as a white crystalline solid, m.p. 181.5-183°; ir (potassium bromide): 1690, (sh) 1679 cm^{-1} (C=O), 3300-2700 cm^{-1} (NH), 1273-1205 cm^{-1} (CF_3); nmr (DMSO-d_6, TMS) δ: 2.46 (3, s, SCH_3), 3.30 (3, s, NCH_3), 9.33 (1, broad s, exchanges with deuterium oxide, N*H*).

Anal. Calcd. for $C_7H_7F_6N_3OS$: C, 28.48; H, 2.39; N, 14.23; S, 10.86. Found: C, 28.30; H, 2.45; N, 14.28; S, 10.76.

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