18864-77-2; **5** (*o*-Ip), 19103-10-7; **6**, 32414-35-0; **7**, 32388-64-0; Li, 7439-93-2; Na, 7440-23-5; K, 7440-09-7; isopropyl chloride, 75-29-6; isopropyl bromide, 75-26-3; isopropyl iodide, 75-30-9; *N*-benzhydryl-*N*-isopropylaniline, 32388-68-4; *m*-bromoisopropylbenzene, 5433-01-2; *m*-isopropylbenzoic acid, 5651-47-8; *p*-isopropylbenzophenone, 18864-76-1, 32388-72-0 (2,4-DNPH); *m*-isopropylbenzophenone, 32388-73-1; 2,5-diisopropylbenzophenone, 2887-73-2; *m*-isopropylbenzophenone anil, 32388-75-3; 2,5-diisopropylbenzophenone anil, 32388-64-0; *N*-(*m*-isopropylbenzhydryl)-aniline, 32388-78-6.

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Notes

Reactions of Some Dithiazolium Cations with Potassium Cyanate

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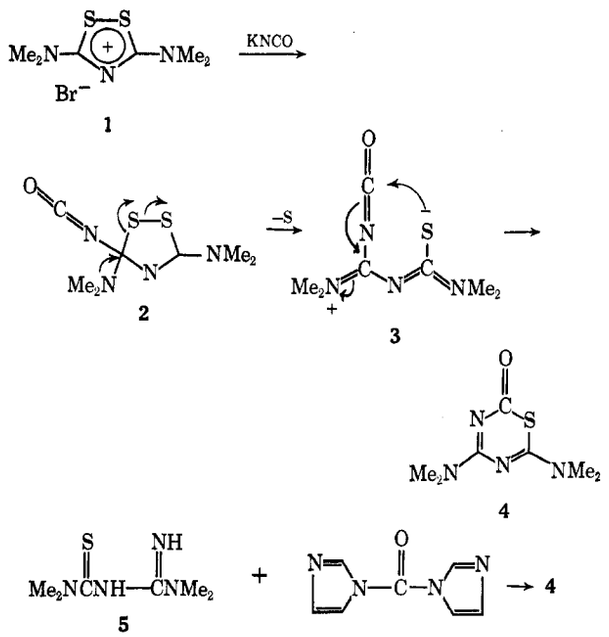
In the course of our studies of 3,5-disubstituted 1,2,4-dithiazolium salts as insect chemosterilants,[1] we recently found that 3,5-bis(dimethylamino)-1,2,4-dithiazolium bromide (**1**) and several related dithiazolium salts react with sodium azide in DMF or DMSO to provide 3,5-disubstituted 1,2,4-thiadiazoles.[2] Cyanate ion, like azide, is a nucleophile that contains a potential electrophilic center, and we felt that, if ring opening of **1** could be initiated by KNCO, a reaction similiar to the NaN_3 addition should occur except that in this case a six-membered ring would result. Indeed, when **1** and KNCO were allowed to react in refluxing DMF, a neutral compound was obtained (71%) that has been identified by its elemental analysis, ir, nmr, and mass spectra as 4,6-bis(dimethylamino)-2*H*-1,3,5-thiadiazin-2-one (**4**). Final confirmation of structure came from an alternate synthesis achieved by condensing 3-(*N*,*N*-dimethylamidino)-1,1-dimethyl-2-thiourea[1,2] (**5**) with carbonyldiimidazole in refluxing toluene (Scheme I).

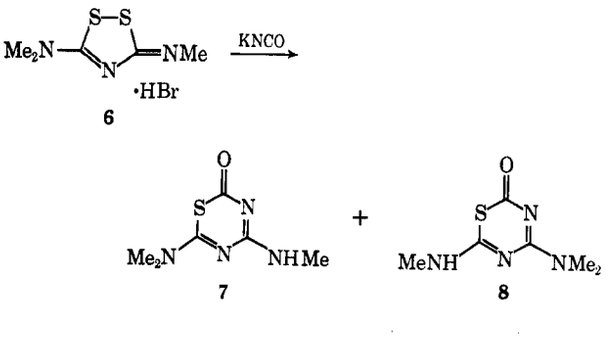
The nmr signals of the methyl hydrogens of dimethylamides and related compounds are frequently observed as doublets because of restricted rotation around the N–C bonds.[3] Both of the dimethylamino signals of **7** appear as doublets at room temperature (coalescence temperatures in chlorobenzene *ca.* 45 and 87°). This constitutes an interesting extension of the dialkylamide phenomenon, as in this case the carbonyl group is in a heterocyclic ring. We assume, without evidence, that the 4-dimethylamino group has the larger rotation barrier.

SCHEME I



3,5-Dipiperidino- and 3,5-bis(1-pyrrolidinyl)-1,2,4-dithiazolium bromides reacted analogously with KNCO to give 4,6-dipiperidino- and 4,6-bis(1-pyrrolidinyl)-2*H*-1,3,5-thiadiazin-2-ones in 40–88% yield (few attempts were made to optimize conditions or yields). Thus it appears that this constitutes a general synthesis of 4,6-bis(dialkylamino)-1,3,5-thiadiazin-2-ones, a previously unreported class of compounds.

5-(Dimethylamino)-3-(methylimino)-3*H*-1,2,4-dithiazole hydrobromide (**6**) reacted with NaN_3 to give 5-

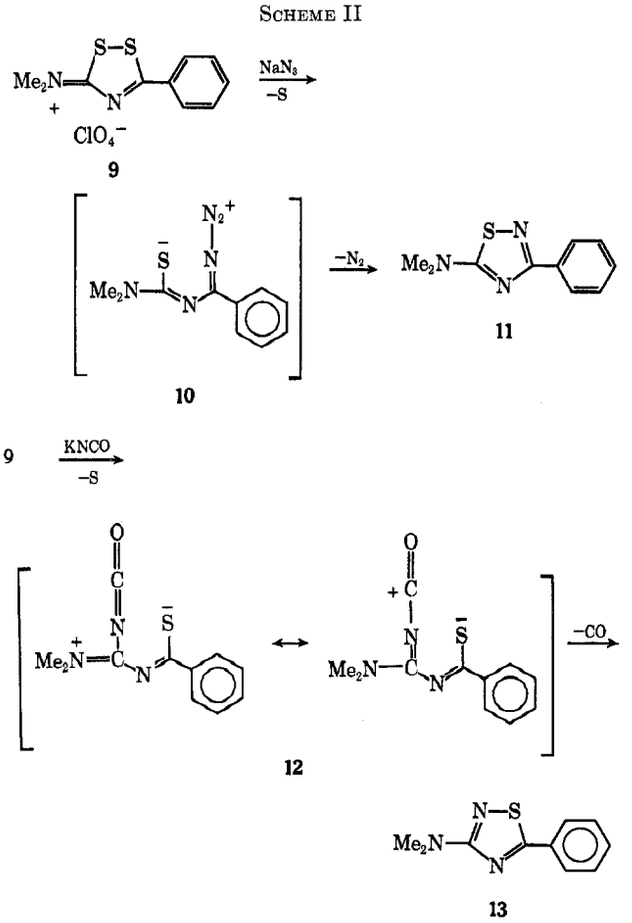


(1) J. E. Oliver, S. C. Chang, R. T. Brown, J. B. Stokes, and A. B. Borkovec, *J. Med. Chem.*, in press.
(2) J. E. Oliver, *J. Org. Chem.*, **36**, 3465 (1971).
(3) W. E. Stewart and T. H. Siddall, III, *Chem. Rev.*, **70**, 517 (1970).

(dimethylamino)-3-(methylamino)-1,2,4-thiadiazole.[2] The reaction of **6** with KNCO was more complex, and both **7** and **8** were obtained along with an unidentified material. The two isomers were obtained pure only with considerable difficulty (column chromatography followed by repeated fractional recrystallization), and the exact ratio of the two isomers in the reaction mixture is unknown. Their high-resolution mass spectra allowed us to assign structures **7** and **8** to the major and minor isomers, respectively. Thus the major product corresponds to attack by cyanate at C-3 of **6**, as was the case in the NaN_3 reaction, where the only observed product also resulted from attack at C-3.

An interesting but unexplained contrast between the NaN_3 and KNCO additions was provided by the reactions of these reagents with 3-(dimethylamino)-5-phenyl-1,2,4-dithiazolium perchlorate (**9**). 5-(Dimethylamino)-3-phenyl-1,2,4-thiadiazole (**11**) was the only isolated product from **9** and NaN_3.[2] When **9** was treated with KNCO in DMF or DMSO, the product was not a 1,3,5-thiadiazin-2-one, but instead was 3-(dimethylamino)-5-phenyl-1,2,4-thiadiazole (**13**, 76–83% yield). This unexpected product is best explained by assuming that carbon monoxide was eliminated from **12** in the same manner that nitrogen was lost from **10** (Scheme II). Thiadiazole **13** is a result of

SCHEME II



cyanate addition to the 3 position of **9**, whereas thiadiazole **11** resulted from azide addition to the 5 position of **9**. Thus, although it appears that similar mechanisms can explain the reactions of cyanate and azide anions with dithiazolium cations, the two reagents do not necessarily add to the same positions. Whether potassium *vs.* sodium counterions influenced this difference has not been investigated, but, if, as seems likely, ion exchange (*e.g.*, formation of a dithiazolium cyanate salt) precedes the nucleophilic attack, the presence of sodium or potassium bromide or perchlorate would not be expected to have much effect.

Potassium thiocyanate could not be made to undergo an analogous reaction with **1**; the only product that could be identified was the thiocyanate salt of cation **1**.[4] This thiocyanate salt was remarkably stable; indeed, it was recovered unchanged after 45 min in a sealed tube at 215°, and, upon attempted pyrolysis in a sublimation apparatus (250°, 0.05 mm), an oily sublimate was collected whose infrared spectrum was essentially identical with that of the starting thiocyanate salt.

As was the case with the NaN_3 reaction, deeply colored reaction mixtures often resulted when a dithiazolium salt and KNCO were heated together in DMF or DMSO, but again there were a few instances in which shades deeper than yellow did not develop. Since a variety of sulfur compounds produce colors with NaN_3 in DMF,[2] we feel that the colors observed here were probably not directly associated with these specific reactions.

Experimental Section[5]

Melting points are uncorrected. Nuclear magnetic resonance spectra were recorded on a Varian Model T-60 spectrometer except for the variable temperature spectra which were recorded on a Varian A-60 spectrometer. Mass spectra were recorded on a Finnigan Model 1015 Quadrupole mass spectrometer or on a Consolidated Electrodynamics Corp. Model 21-110B high resolution mass spectrometer. Infrared spectra were obtained on a Perkin-Elmer Model 137 sodium chloride prism spectrophotometer. Magnesium sulfate was employed as a drying agent. DMSO and DMF were stored over molecular sieves but were not otherwise purified. A high-vacuum rotary evaporator with a CO_2 trap was employed to remove DMF. The preparation of the dithiazolium salts has been reported.[1,2,4] Microanalyses were preformed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Reactions of 3,5-Bis(dialkylamino)-1,2,4-dithiazolium Bromides with Potassium Cyanate. 4,6-Bis(dimethylamino)-2*H*-1,3,5-thiadiazin-2-one (4).—A mixture of 3,5-bis(dimethylamino)-1,2,4-dithiazolium bromide (**1**, 8.10 g) and KNCO (2.52 g) in DMF (50 ml) was refluxed under N_2 for 40 min, then was stirred overnight at room temperature. The mixture was filtered and the filtrate was stripped *in vacuo*. The residue was extracted with hot MeOH (to remove sulfur), the MeOH solution was filtered and evaporated, and the residue was extracted with several portions of hot CCl_4 (total 150 ml). The filtered CCl_4 solution was chilled and **4** separated as a white solid (4.25 g, 71%, mp 132–133°). The analytical sample (CCl_4) had mp 135.5–136°; ir ($CHCl_3$) 1160, 1550, 1400, 1375, cm^{-1}; nmr (C_6H_5Cl) δ 2.70 and 2.80 (poorly resolved at 37°, coalesce to a singlet at *ca.* 45°), 2.88 and 3.04 (sharp singlets at 37°, coalesce to a single peak at *ca.* 87°); mass spectrum (70 eV) *m/e* (rel intensity) 200 (30, parent ion), 172 (44, M − CO), 156 (72, M − Me_2N), 88 (32, $Me_2NC{=}S^+$), 70 (100, Me_2NCN^+).

Anal. Calcd for $C_7H_{12}N_4OS$: C, 41.97; H, 6.04; N, 27.98; S, 16.01. Found: C, 41.76; H, 6.02; N, 27.85; S, 16.19.

4,6-Dipiperidino-2*H*-1,3,5-thiadiazin-2-one was obtained by heating 3.50 g of 3,5-dipiperidino-1,2,4-dithiazolium bromide with 0.81 g of KNCO in DMSO (25 ml) at 115–120° for 1 hr. The mixture was cooled and poured into cold water. A solid separated that was collected and taken up in 1:1 MeOH–EtOH. The solution was filtered and evaporated, and the residue was re-

(4) W. R. Diveley, U. S. Patent 3,166,564 (Jan 19, 1965); *Chem. Abstr.*, **62**, 9145*g* (1965).

(5) Mention of a proprietary product or company does not necessarily imply endorsement by the U. S. Department of Agriculture.

crystallized from isooctane–EtOAc to give 2.47 g (88%) of 4,6-dipiperidino-2*H*-1,3,5-thiadiazin-2-one, mp 133–138°. Recrystallization from EtOH–H_2O and then heptane–EtOAc gave the pure material: mp 141–142°; ir ($CHCl_3$) 1650, 1523, 1440, 1410 cm^{-1}.

Anal. Calcd for $C_{13}H_{20}N_4OS$: C, 55.68; H, 7.19; N, 19.98; S, 11.44. Found: C, 56.01; H, 7.15; N, 20.17; S, 11.20.

4,6-Bis(1-pyrrolidinyl)-2*H*-1,3,5-thiadiazin-2-one was prepared by refluxing 3,5-bis(1-pyrrolidinyl)-1,2,4-dithiazolium bromide (3.23 g) and KNCO (0.86 g) in DMF (25 ml) for 1 hr. The DMF was stripped and the residue was extracted into MeOH. The MeOH extract was filtered and evaporated and the residue was extracted with hot EtOAc. Dilution of the EtOAc solution with hexane and chilling precipitated the product as a light tan solid (1.19 g, 40%, mp 133–137°). Recrystallization from EtOAc gave 0.80 g, mp 140–141°; ir ($CHCl_3$) 1650, 1530, 1410 cm^{-1}.

Anal. Calcd for $C_{11}H_{16}N_4OS$: C, 52.35; H, 6.39; N, 22.20. Found: C, 52.45; H, 6.21; N, 22.21.

Synthesis of 4 from 3-[*N*,*N*-(Dimethylamidino)]-1,1-dimethyl-2-thiourea[1] (5) and Carbonyldiimidazole.—A solution of **5** (258 mg) and 1,1-carbonyldiimidazole (240 mg) in toluene (12 ml) was refluxed for 4 hr, cooled, washed with H_2O, dried, and evaporated. The residue (40 mg, mp 124–129°) was recrystallized from CCl_4 to give pure **4**, mp 135–136°, shown by its infrared spectrum and by mixture melting point to be identical with that prepared from **1** and KNCO.

Reaction of 5-(Dimethylamino)-3-(methylimino)-3*H*-1,2,4-dithiazole Hydrobromide (6) with Potassium Cyanate.—A mixture of **6** (5.00 g) and KNCO (1.74 g) in DMF (50 ml) was refluxed under N_2 for 1 hr. After cooling to room temperature the mixture was filtered and the filtrate was stripped. The residue (in CH_2Cl_2) was added to a silica gel column. Elution with C_6H_6 gave 1 g of an unidentified yellow solid, mp 140–177°, that moved with the solvent front. The column was then eluted with $CHCl_3$–C_6H_6 and finally with $CHCl_3$. 6-(Dimethylamino)-4-(methylamino)-2*H*-1,3,5-thiadiazin-2-one (**7**) and 4-(dimethylamino)-6-(methylamino)-2*H*-1,3,5-thiadiazin-2-one (**18**) were eluted together over a series of fractions (as judged by nearly identical ir spectra of early and late fractions). The evaporated fractions were combined in hot CH_3CN; chilling the solution gave 0.80 g (22%) of a whilte solid, mp 185–195°. Several recrystallizations from EtOH and then CH_3CN gave pure **7**, mp 188–189°; ir (KBr) 1695, 1620, 1560, 1515, 1480, 985 cm^{-1}; nmr (DMSO-d_6) δ 3.11 (s, 6 H), 3.50 (s, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 186 (100, molecular ion), 158 (22, M − CO), 113 (28), 88 (10), 84 (21), 83 (30). High-resolution analysis of the *m/e* 88 area showed two peaks with exact molecular weights 88.0100 and 88.0223 (calcd for $C_2H_4N_2S$ and C_3H_6NS, respectively, 88.0095 and 88.0221). The latter peak, absent in the spectrum of **8**, corresponds to $Me_2NC{=}S^+$ which could only have been derived from structure **7**.

Anal. Calcd for $C_6H_{10}N_4OS$: C, 38.69; H, 5.41; N, 30.08; S, 17.22. Found: C, 38.56; H, 5.29; N, 29.87; S, 17.42.

Crude **8** was obtained from the mother liquors of **7**; the analytical sample was obtained by repeated recrystallizations (three from EtOH, then two from CH_3CN), mp 218–220°; ir (KBr) 1665, 1610, 1510, 1430, 1260, 1110, 1020, 863 cm^{-1}; nmr (DMSO-d_6) δ 3.11 (s, 6 H) and 3.52 (s, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 186 (100, molecular ion), 113 (34), 98 (14), 83 (11), 71 (10).

Anal. Calcd for $C_6H_{10}N_4OS$: C, 38.69; H, 5.41; N, 30.08; S, 17.22. Found: C, 38.92; H, 5.44; N, 30.33; S, 17.25.

Reaction of 3-(Dimethylamino)-5-phenyl-1,2,4-dithiazolium Perchlorate (9)[2] and KNCO.—A mixture of **9** (5.00 g) and KNCO (1.47 g) was heated for 0.5 hr in refluxing DMF (100 ml). The solution was cooled to room temperature, filtered, and stripped, and the residue was chromatographed on silica gel. 5-(Dimethylamino)-3-phenyl-1,2,4-thiadiazole (**13**) was quickly eluted with petroleum ether (bp 30–60°) and was obtained as a clear oil that solidified on standing (2.62 g, 83%). A portion was sublimed *in vacuo* and then recrystallized from MeOH–H_2O, mp 46°; ir ($CHCl_3$) 1540, 1410, 1340, 975, 885 cm^{-1}; nmr ($CDCl_3$) δ 3.25 (s, 6, Me_2N) 7.33–7.60 (m, 3, Ph), 7.84–8.17 (m, 2, Ph); mass spectrum (70 eV) *m/e* 205 (100, parent ion), 121 (12, $PhC{=}S^+$). The isomeric 3-(dimethylamino)-5-phenyl-1,2,4-thiadiazole has mp 89°.[2,6]

The same product was obtained by reacting **9** and KNCO in DMSO (100°, 45 min); the reaction mixture was partitioned between C_6H_6 and H_2O and **13** was obtained in 76% yield upon evaporation of the C_6H_6 solution.

Anal. Calcd for $C_{10}H_{11}N_3S$: C, 58.51; H, 5.40; N, 20.47. Found: C, 58.30; H, 5.35; N, 20.31.

Registry No.—**4**, 32251-48-2; **7**, 32251-49-3; **8**, 32304-28-2; **13**, 32251-50-6; 4,6-dipiperidino-2*H*-1,3,5-thiadiazin-2-one, 32251-51-7; 4,6-bis(1-pyrrolidinyl)-2*H*-1,3,5-thiadiazin-2-one, 32251-52-8.

Acknowledgment.—We thank Professor C. Storm of Howard University for the variable-temperature nmr spectra.

(6) J. Goerdeler and K. H. Heller, *Chem. Ber.*, **97**, 225 (1964).

Nuclear Magnetic Resonance Spectroscopy. Effect of *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine on the Schlenk Equilibrium of Ethylmagnesium Bromide[1]

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The composition of Grignard reagents has been studied extensively by nuclear magnetic resonance spectroscopy and other physical techniques.[3] Recently Parris and Ashby,[4] using nmr spectroscopy, observed both dialkyl- and alkylmagnesium species in Grignard solutions from methyl and *tert*-butyl halides. Earlier Evans and coworkers[5] had observed diarylmagnesium and arylmagnesium halides by both fluorine and proton magnetic resonance. We wish to report the observation of diethylmagnesium and ethylmagnesium bromide in tetrahydrofuran solutions containing *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.

The proton magnetic resonance spectrum of the Grignard reagent prepared from ethyl bromide and magnesium is a typical A_2X_3 type spectrum. The resonances of both the methyl, 1.11 ppm downfield from external tetramethylsilane, and methylene protons, 0.78 ppm upfield, are easily distinguished from those of the solvent. A small quantity of ethane is usually formed from trace amounts of moisture. Spectra obtained at temperatures down to −70° exhibited no change other than slight loss in resolution. Variable-temperature spectra of the methylene protons of 0.33 *M* ethylmagnesium bromide in tetrahydrofuran, which is 0.18 *M* in *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, are shown in Figure 1. Broadening of the resonance occurs when lowering the temperature and, at −50°, the methylene proton resonances appear as overlapping

(1) Taken from the Ph.D. Dissertation of J. A. Magnuson, 1968. Supported by the National Science Foundation.

(2) National Defense Education Act Fellow, 1965–1967.

(3) For recent review articles, see the following and other volumes in series: (a) J. P. Oliver, *Advan. Organometal. Chem.*, **8**, 167 (1970); (b) D. Seyferth, *Organometal. Chem. Rev., Sect. B*, **3**, 37 (1967); (c) B. J. Wakefield, *Organometal. Chem. Rev.*, **1**, 131 (1966); (d) E. C. Ashby, *ibid.*, **5**, 225 (1969).

(4) G. E. Parris and E. C. Ashby, *J. Amer. Chem. Soc.*, **93**, 1206 (1971).

(5) (a) D. F. Evans and M. S. Kahn, *J. Chem. Soc. A*, 1643 (1967); (b) D. F. Evans and M. S. Kahn, *ibid.*, 1648 (1967); (c) D. F. Evans and V. Fazakerly, *Chem. Commun.*, 974 (1968).