

Reaction of Grignard Reagents with Tetramethylthiuram Disulfide¹

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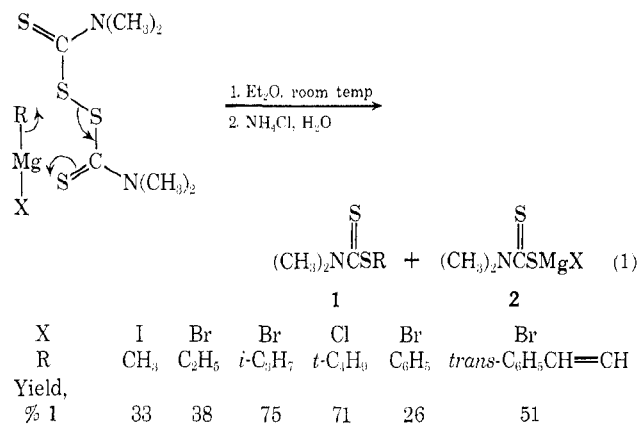
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Alkyl, alkenyl, and aryl Grignard reagents react with tetramethylthiuram disulfide to produce the corresponding dimethyldithiocarbamate esters. The spectral properties of the esters are discussed.

The object of this research was to find an alternative synthesis of dithiocarbamate esters. Since tetramethylthiuram disulfide (TMTD) suffers a displacement reaction at sulfur when it is treated with nucleophiles, such as cyanide ion² or amines,³ the reaction between TMTD and Grignard reagents was investigated.

A general, preparatively useful reaction was discovered. Primary, secondary, and tertiary alkyl, alkenyl, and aryl Grignard reagents react with TMTD to form the corresponding dithiocarbamate esters 1 (eq 1). The synthetic advantages of this reaction are



clear. It represents the most convenient and least hazardous procedure for preparing *t*-alkyl, alkenyl, and aryl esters. For example, phenyl dimethyldithiocarbamate was previously prepared by the reaction between phenyldiazonium ion and dimethyldithiocarbamate ion,⁴ while vinyl diethyldithiocarbamate was synthesized by the high-pressure reaction of diethylamine, carbon disulfide, and acetylene.⁵

Reaction 1 is carried out by adding solid TMTD to an ethereal solution of the Grignard reagent. The mechanism of this exothermic reaction probably involves a displacement reaction at sulfur, and apparently the driving force is the formation and precipitation of the magnesium dithiocarbamate salt 2.

The esters were identified by their spectral properties. The infrared spectra showed a strong 1500-cm⁻¹ band, which is consistent with the N=C=S group frequency.⁶ The mass spectra reveal the esters as having intense molecular ions and a base peak at *m/e* 88, which corresponds to the structure (CH₃)₂N⁺=

C=S.⁷ The nuclear magnetic resonance spectra are consistent with all proposed structures. The assignment of *trans* isomerism for styryl dimethyldithiocarbamate rests on the coupling constant (*J* = 16 Hz) for the vinyl hydrogens. The methyl groups substituted on nitrogen are equivalent for each ester. However, the spectrum of dimethylthiobenzamide displays nonequivalent methyl groups at the same temperature. Evidently the electron-donating ability of the thiol sulfur atom of dithiocarbamates serves to decrease the amount of double-bond character of the carbon-nitrogen bond relative to that of the thioamide and thus decreases the rotational barrier about the bond. This behavior is consistent with that observed for dialkylcarbamates and amides.⁸

Experimental Section⁹

Methyl Dimethyldithiocarbamate.¹⁰—Methylmagnesium iodide (0.20 mol) was prepared from 4.92 g (0.20 g-atom) of magnesium metal and 30.14 g (0.21 mol) of iodomethane in 250 ml of dry ether. By means of Gooch tubing 24.06 g (0.10 mol) of TMTD was added slowly. The reaction mixture was stirred for 1 hr and then was poured into 500 ml of a cold aqueous saturated solution of NH₄Cl. The ether was separated, dried (MgSO₄), and evaporated. The crude white crystals were chromatographed on 200 g of Merck acid-washed aluminum oxide and eluted with hexane and then with benzene. This gave 4.5 g (33%) of the dithiocarbamate, mp 45–47° (lit.¹⁰ mp 45–46°). An analytical sample was prepared by sublimation at 25° (0.02 mm): uv max (95% EtOH) 221 mμ (ε 10,800), 247 (9240), 273 (11,780), and 318 (584); ir (CHCl₃) 2980, 2925, 1500, 1380, 1260, 1150, 1060, 1010, 990, 965, and 570 cm⁻¹; nmr (CDCl₃) δ 2.72 (s, 3) and 3.58 (s, 6); mass spectrum (80 eV), *m/e* (relative intensity), 120 (2), 91 (15), 88 (100), 73 (22), 47 (7), 45 (18), 44 (29), and 42 (27). *Anal.* Calcd for C₄H₉NS₂: C, 35.52; H, 6.71; N, 10.35; S, 47.42. Found: C, 35.38; H, 6.68; N, 10.39; S, 47.21.

Ethyl Dimethyldithiocarbamate.¹¹—Ethylmagnesium bromide (0.25 mol) was treated with 24.11 g (0.10 mol) of tetramethylthiuram disulfide as described above. After addition of aqueous NH₄Cl solution, the mixture was filtered and the precipitate was washed with ether. The ether was evaporated giving a crude brown oil, which was distilled giving 5.7 g (38%) of the dithiocarbamate: bp 55–57° (0.05 mm); mp +2.0° (lit.¹¹ mp +2.0°); uv max (95% EtOH) 222 mμ (ε 9920), 248 (9010), and 277 (10,450); ir (CHCl₃) 2980, 2940, 3880, 1500, 1390, 1280, 1260, 1150, 1060, 990, 880, and 570 cm⁻¹; nmr (CDCl₃) δ 1.38 (t, 3, *J* = 7.5 Hz), 3.48 (q, 2, *J* = 7.5 Hz), and 3.55 (s, 6); mass

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spectrum (80 eV), m/e (relative intensity) 149 (33), 134 (3), 121 (16), 120 (15), 106 (30), 105 (35), 91 (56), 88 (100), 77 (22), 73 (18), 57 (32), 55 (36), 44 (27), 43 (74), 42 (45), 41 (76), and 39 (60).

Isopropyl Dimethyldithiocarbamate.¹²—Isopropylmagnesium bromide (0.20 mol) was treated with 24.14 g (0.10 mol) of tetramethylthiuram disulfide. After addition of aqueous NH_4Cl , the ether solution was filtered, dried (MgSO_4), and evaporated to give 12.3 g (75%) of a light brown oil, which distilled to give the colorless dithiocarbamate: bp 67–69° (0.08 mm) (lit.¹³ 126° (12 mm)); uv max (95% EtOH) 223 $m\mu$ (ϵ 12,830), 248 (11,620), and 277 (13,220); ir (CHCl_3) 2975, 2940, 2880, 1500, 1380, 1265, 1153, 1065, 990, 880, 753, and 580 cm^{-1} ; nmr (CDCl_3) δ 1.45 (d, 6, $J = 7.5$ Hz), 4.05 (septet, 1, $J = 7.5$ Hz) and 3.57 (s, 6); mass spectrum (80 eV), m/e (relative intensity) 163 (52), 121 (31), 120 (11), 88 (100), 73 (13), 44 (15), 43 (18), and 41 (22).

***t*-Butyl Dimethyldithiocarbamate.**—*t*-Butylmagnesium chloride (0.21 mol) was treated with 17.11 g (0.07 mol) of tetramethylthiuram disulfide. After hydrolysis the mass was filtered and the precipitate was washed with ether. The ether was dried (MgSO_4) and evaporated giving 13.5 g of a crude black oil, which was distilled giving 8.2 g (71%) of the yellow dithiocarbamate, bp 60–64° (0.08 mm). When the product was cooled in a Dry Ice-acetone bath, colorless crystals formed. It slowly decomposed to tetramethylthiuram disulfide at room temperature. Therefore a good analysis could not be obtained: uv max (95% EtOH) 222 $m\mu$ (ϵ 8600), 250 (8450), and 280 (9550); ir (CHCl_3) 2975, 2930, 2865, 1500, 1460, 1375, 1260, 1160, 1140, 1060, 995, 870, 595, and 570 cm^{-1} ; nmr (CDCl_3) δ 1.65 (s, 9), and 3.40 (s, 6); mass spectrum (80 eV), m/e (relative intensity) 166 (12), 121 (27), 88 (95), 73 (18), 57 (56), 44 (31), 42 (50), 41 (100), and 39 (58). *Anal.* Calcd for $\text{C}_7\text{H}_{15}\text{NS}_2$: C, 47.35; H, 8.53; N, 7.96; S, 36.16. Found: C, 48.13; H, 8.64; N, 8.09; S, 35.28.

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Phenyl Dimethyldithiocarbamate.⁴—Phenylmagnesium bromide (0.20 mol) was treated with 0.10 mol of tetramethylthiuram disulfide. After hydrolysis the ether was separated, washed, dried (MgSO_4), and evaporated to give a semisolid red oil. Crystallization from cyclohexane gave 5.2 g (26%) of the dithiocarbamate: mp 94–95°; uv max (95% EtOH) 215 $m\mu$ (ϵ 19,600), 243 (12,700), 248 (12,400), and 270 (9200); ir (CHCl_3) 2990, 2940, 1510, 1480, 1450, 1390, 1260, 1150, 990, 870, 690, 570, and 510 cm^{-1} ; nmr (CDCl_3) δ 3.45 (s, 6) and 7.41 (s, 5); mass spectrum (80 eV), m/e (relative intensity) 197 (49), 109 (7), 88 (100), 77 (10), 73 (18), and 42 (11). *Anal.* Calcd for $\text{C}_9\text{H}_{11}\text{NS}_2$: C, 54.78; H, 5.57; N, 7.10; S, 32.51. Found: C, 54.77; H, 5.69; N, 7.06; S, 32.61.

***trans*-Styryl Dimethyldithiocarbamate.**—To *trans*-styrylmagnesium bromide from 0.30 mol of *trans*- β -bromostyrene was added 0.10 mol of tetramethylthiuram disulfide. After the usual work-up the ether solution was evaporated to a semisolid, which was crystallized from benzene-hexane to give 11.0 g (51%) of the dithiocarbamate. An analytical sample was obtained from further recrystallization: mp 93–94°; uv max (95% EtOH) 217 $m\mu$ (ϵ 18,950), 275 (25,100), and 302 (17,420); ir (CHCl_3) 2990, 2940, 2860, 1610, 1550, 1450, 1390, 1260, 1155, 990, 950, 880, 690, 590, and 570 cm^{-1} ; nmr (CDCl_3) δ 3.45 (s, 6), 6.75 (d, 1, $J = 16$ Hz), 7.37 (m, 5), and 7.50 (d, 1, $J = 16$ Hz); mass spectrum (80 eV), m/e (relative intensity), 223 (20), 88 (100), 73 (4), and 42 (3). *Anal.* Calcd for $\text{C}_{11}\text{H}_{13}\text{NS}_2$: C, 59.15; H, 5.86; N, 6.27; S, 28.72. Found: C, 59.26; H, 6.00; N, 6.36; S, 28.15.

Registry No.—Methyl dimethyldithiocarbamate, 3735-92-0; ethyl dimethyldithiocarbamate, 617-38-9; isopropyl dimethyldithiocarbamate, 23885-26-9; *t*-butyl dimethyldithiocarbamate, 23885-27-0; phenyl dimethyldithiocarbamate, 16906-70-0; *trans*-styryl dimethyldithiocarbamate, 23846-99-3; TMTD, 137-26-8.

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Isolation of an Unstable Intermediate in the Reaction of Tetramethyl-3-thio-1,3-cyclobutanedione with Diazomethane

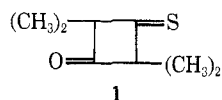
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The reaction of tetramethyl-3-thio-1,3-cyclobutanedione (1) with diazomethane gave 4,4,6,6-tetramethyl-1-thiaspiro[2.3]hexan-5-one (9). An unstable intermediate isolated from this reaction was tentatively assigned the structure of 3,4-diaza-6,6,8,8-tetramethyl-7-oxo-1-thiaspiro[4.3]oct-3-ene (8a) on the basis of infrared and nmr spectra. The thirane ring of 9 was found to be surprisingly unreactive toward nucleophilic and electrophilic reagents, although it could be desulfurized with triphenylphosphine to give 2,2,4,4-tetramethyl-3-methylenecyclobutanone (17) or with Raney nickel to yield 2,2,3,4,4-pentamethylcyclobutanone as the major product. Reduction of 9 with lithium aluminum hydride or sodium borohydride gave a mixture of isomeric alcohols 12, leaving the thirane ring unattacked.

The synthesis of tetramethyl-3-thio-1,3-cyclobutanedione (1) was recently reported.^{1,2} This compound is



one of the few stable aliphatic thio ketones known. It has no tendency to polymerize or dimerize, in contrast to most aliphatic thio ketones.^{3,4} The ready

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availability of 1 allowed studies of the chemistry of an aliphatic thione group without the complications of dimerization, enolization, etc. This account will be limited primarily to a discussion of the reaction of the thione group with diazomethane and to a discussion of the chemistry of the resulting products.

The first report of the reaction between a diazoalkane and a thio ketone was that of Staudinger and Siegwart,⁵ who investigated the reaction between diphenyldiazomethane and various diaryl thio ketones (Scheme I). The reaction resulted in the formation of tetrasubstituted thiranes, which lost sulfur upon heating to give the corresponding ethylenes. Staudinger and Siegwart postulated the formation of an unstable Δ^2 -1,2,3-

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