Notes

Procedure for the Preparation of Pure Dithiocarbamates

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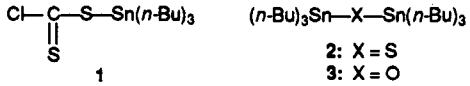
Dithiocarbamates are used as ligands for soft metal complexation and in organic synthesis and are usually prepared by the nucleophilic addition of an amine to carbon disulfide.[1] Since the free acids thus obtained are unstable, the reaction is conducted in the presence of a base, to isolate the corresponding dithiocarbamate salts. Purification is achieved by crystallization but the yields can be very disappointing since the dithiocarbamates may decompose, particularly upon heating. Significantly, yields are usually not given in the literature for these preparations.

For an ongoing research project, the need became apparent for a high-yielding preparative procedure for securing pure dithiocarbamate salts with temporary protection of this functional group to permit purification. Such an approach does not seem to have been previously considered, and our results are presented in this note.

An appropriate dithiocarbamate protecting group should fulfill two criteria: (1) it should be readily introduced and permit easy purification when necessary, (2) its removal should yield the pure dithiocarbamate directly, *without* further purification.

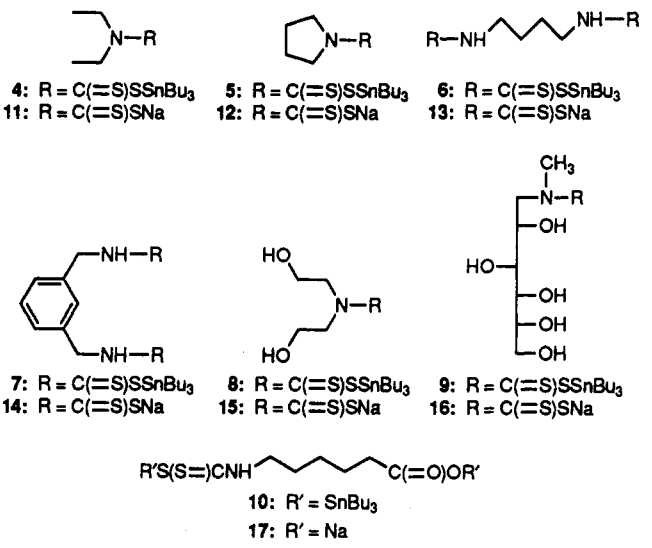
Stannyl esters of carboxylic acids have received limited attention in synthetic chemistry in spite of their relative stability and facile cleavage under appropriate conditions.[2,3] This balance between stability and ease of cleavage[2] seemed, after examination of other possibilities among the group IV_b elements, to be a good starting point for our purposes.

Our early efforts to obtain stannyl dithiocarbamates involved the condensation of an amine with tributyltin dithiochloroformate (1). Unfortunately, 1 could not be prepared using a variety of approaches previously successful with alkyl dithiochloroformates,[4,5] suggesting unstability during its formation. Noteworthy is that tributyltin chloride was formed from reaction of bis(tributyltin) sulfide (2)[6] with thiophosgene while *in situ* quenching at



1 2: X = S 3: X = O

−78 °C of this reaction mixture[7] with diethylamine resulted in the isolation of diethylamine hydrochloride. Known literature preparations of stannyl dithiocarbamates involve condensations of dithiocarbamic salts with a halo stannane,[8,9] insertion of carbon disulfide into a stannylamine,[10] oxygen/sulfur exchange from stannyl carbamates,[11] alkyltin hydride reduction of cyanomethyl derivatives,[12] or silicon/tin exchange in dithiocarbamate esters.[13] The desired stannyl dithiocarbamates 4–10 could be obtained directly from the corresponding amines (R = H), in 80–95% yield, by the known reaction of carbon disulfide in the presence of 0.5 equiv of 3.[8,9] It is of particular interest that the yields with diamines (to give 6 and 7) are good, and that this method is compatible with the presence of hydroxyl groups (see 8 and 9). In the case of an amino acid, 1 mol equiv of the tin oxide 3 was required. 10 was thus obtained from 6-aminocaproic acid, since the stannyl ester of the carboxyl group was also formed simultaneously. Given the known sensitivity of tin compounds to silica gel,[14,15] the stannyl dithiocarbamates were purified on neutral alumina, except for 10.[16]



Stability studies were performed with 4 which proved to be stable to water, alcohols, amines (NH_3 or *tert*-butylamine), and even a strong non-nucleophilic base (lithium diisopropylamide). The structures of 4–10 were

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(9) Srivastava, T. N.; Kumar, V. *J. Organometal. Chem.* **1976**, *107*, 55–61.
(10) George, T. A.; Jones, K.; Lappert, M. F. *J. Chem. Soc.* **1965**, 2157–2165.
(11) Dalton, R. F.; Jones, K. *J. Chem. Soc.* (A) **1970**, 590–594.
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(13) Tyurina, L. A.; Kuznetsova, G. V.; Semenov, V. A.; Malkova, T. I.; Voronkov, M. G.; Mirskov, R. G. *Zh. Obshch. Khim.* **1984**, *54*, 1559–1566 (Engl. transl. 1387–1393).
(14) Farina, V. *J. Org. Chem.* **1991**, *56*, 4985–4987.
(15) A blackish color developed rapidly when attempting purifications of these esters on silica gel.
(16) Compound 10 is the sole reaction product but was not purified to avoid deprotection of the carboxylate tin ester during chromatography; it could be used satisfactorily as such for the subsequent deprotection step.

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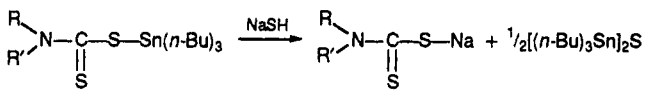
readily assigned from unambiguous NMR resonances; in addition to the thiocarbonyl group at 194–201 ppm,[17,18] diagnostic peaks are the downfield-shifted resonances of the CH_2N (5–9 ppm for ^{13}C and 0.4–0.9 ppm for ^1H) in comparison with those of the starting amines. $^{119,117}Sn$ couplings with ^{13}C (^1J = 330–348 Hz, ^2J = 20–22 Hz, ^3J = 66–68 Hz) were in accord with literature value.[17,19,20]

Having the pure dithiocarbamates precursors in hand, an efficient method for their conversion to the corresponding acid salts was next sought. Basic medium such as NaOH or LiOH did produce the desired dithiocarbamates, but only in fair yield. Fluoride-based reagents, such as NaF and CsF, which are known for their affinity for tin,[3,21-24] led to little improvement: unidentified material always accompanied the desired dithiocarbamates. A clean reaction occured with ammonium fluoride, but gave the corresponding amine fluoride through concomitant loss of carbon disulfide.

The use of sodium hydrogen sulfide, however, brought an efficient solution to this problem. The desired dithiocarbamates 11–17[25-29] could, in every case, be obtained quantitatively. The concomitant formation of 2 which was isolated and compared with an authentic sample,[6] led to the net reaction:



Experimental Section

Melting points were taken on a hot plate microscope apparatus and are not corrected. NMR spectra were taken at 200 MHz (^1H) and 50 MHz (^{13}C). Standard abbreviations are used for description of spectra with m for multiplet and M for unresolved multiplet. The residual absorption of the NMR solvent was taken as the reference except for ^{13}C NMR in water. Microanalyses were performed by the Service Central d'Analyses du CNRS, Vernaison, France.

Preparation of Tributyltin Esters. A solution of the amine (R = H) (1 equiv) in chloroform (or methanol in the case of **9** and **10**) (0.4 mL/mmol) was added dropwise to a precooled (<−20 °C) solution of carbon disulfide (1.5 equiv) and bis(tributyltin) oxide (0.5 equiv) in chloroform (5 mL/equiv). After the addition, the cooling bath was removed and the reaction mixture was stirred for an additional 2 h. The volatiles were then removed under reduced pressure at room temperature and the resulting crude reaction mixture was purified by chromatography on neutral alumina (Brockmann activity 1), the solvent system used for elution of each pure compound being indicated below.

Tributyltin diethyldithiocarbamate (4):[30] eluent, dichloromethane/cyclohexane 3:1; oil, 88%; ^1H-NMR ($CDCl_3$) δ 3.85 (q, J = 7.2 Hz, 4H, CH_2N), 1.8–1.0 (M, 24H), 0.85 (t, J = 7.7 Hz, 9H, $Sn(CH_2)_3CH_3$); ^{13}C-NMR ($CDCl_3$) δ 197.2 (C=S), 49.3 (CH_2N), 28.6 (J_{CSn} = 21 Hz, CH_2CH_2Sn), 26.8 (J_{CSn} = 67 Hz, $CH_2(CH_2)_2Sn$), 17.4 (J_{CSn} = 336 Hz, CH_2Sn), 13.5 ($Sn(CH_2)_3CH_3$), 11.8 (NCH_2CH_3).

Tributyltin 1,4-butanediyldithiocarbamate (5):[9] eluent, dichloromethane/cyclohexane 4:1; oil, 97%; ^1H-NMR ($CDCl_3$) δ 3.7 (distorted t, 4H, CH_2N), 1.9 (distorted t, 4H, CH_2CH_2N), 1.8–1.0 (M, 18H), 0.8 (t, J = 7.7 Hz, 9H, $Sn(CH_2)_3CH_3$); ^{13}C-NMR ($CDCl_3$) δ 193.9 (C=S), 54.2 (CH_2N), 28.6 (J_{CSn} = 21 Hz, CH_2CH_2Sn), 26.8 (J_{CSn} = 68 Hz, $CH_2(CH_2)_2Sn$), 26.1 (CH_2CH_2N), 17.1 (J_{CSn} = 334 Hz, CH_2Sn), 13.4 (CH_3).

Bis(tributyltin) 1,4-butanediylbis(dithiocarbamate) (6) eluent, dichloromethane/methanol 9:1; oil, 90%; ^1H-NMR ($CDCl_3$) δ 7.9 (broad t due to NH exchange, 2H), 3.5 (m, 4H, CH_2N), 1.8–0.9 (M, 36H), 0.8 (t, J = 7.7 Hz, $Sn(CH_2)_3CH_3$); ^{13}C-NMR ($CDCl_3$) δ 200.4 (C=S), 47.8 (CH_2N), 28.5 (J_{CSn} = 22 Hz, CH_2CH_2Sn), 26.8 (J_{CSn} = 66 Hz: $CH_2(CH_2)_2Sn$), 25.4 (CH_2CH_2N), 16.9 (J_{CSn} = 330 Hz, CH_2Sn), 13.4 (CH_3). Anal. Calcd for $C_{30}H_{64}N_2S_4Sn_2$: C, 44.02; H, 7.88; N, 3.42. Found: C, 43.87; H, 8.18; N, 3.26.

Bis(tributyltin) xylylenebis(dithiocarbamate) (7): eluent, dichloromethane/methanol 9:1, oil, 83%; ^1H-NMR ($CDCl_3$) δ 7.75 (broad t due to NH exchange, 2H), 7.35–7.1 (M, 4H, aromatics), 4.65 (d, J = 7.2 Hz, 4H, CH_2N), 1.7–1.1 (M, 36H), 0.85 (t, J = 7.7 Hz, 18H, $Sn(CH_2)_3CH_3$); ^{13}C-NMR ($CDCl_3$) δ 200.7 (C=S), 136.8 (C_{ipso}), 129.1, 127.4, and 127.3 (other aromatics), 52.3 (CH_2N), 28.6 (J_{CSn} = 21 Hz, CH_2CH_2Sn), 26.9 (J_{CSn} = 66 Hz, $CH_2(CH_2)_2Sn$), 17.0 (J_{CSn} = 344 Hz, CH_2Sn), 13.5 (CH_3) Anal. Calcd for $C_{34}H_{64}N_2S_4Sn_2$: C, 47.12; H, 7.44; N, 3.23. Found: C, 46.78; H, 7.85; N, 3.52.

Tributyltin bis(2-hydroxyethyl)dithiocarbamate (8): eluent, dichloromethane/methanol 9:1; oil, 82%; ^1H-NMR ($CDCl_3$) δ 4.9 (large s, 2H), 4.1–3.7 (M, 8H, CH_2N and CH_2O), 1.7–0.9 M, 18 H), 0.75 (t, J = 7.7 Hz, 9H, $Sn(CH_2)_3CH_3$); ^{13}C-NMR δ 200.0 (C=S), 60.0 and 59.4 (CH_2O and CH_2N), 28.4 (J_{CSn} = 21 Hz, CH_2CH_2Sn), 26.7 (J_{CSn} = 66 Hz, $CH_2(CH_2)_2Sn$), 17.1 (J_{CSn} = 334 Hz, CH_2Sn), 13.3 (CH_3). Anal. Calcd for $C_{17}H_{37}NO_2S_2Sn$: C, 43.41; H, 7.93; N, 2.98. Found: C, 43.81; H, 8.20; N, 2.78.

Tributyltin *N*-methyl-(D-*gluco*-2,3,4,5,6-pentahydroxyhex-1-yl)dithiocarbamate (9): eluent, dichloromethane/methanol 8:2; mp 82–84 °C, 83%; $[\alpha]^{20}_D$ −9.7° (c = 1.54, $CHCl_3$); ^1H-NMR ($CDCl_3$) δ 4.9–3.5 (M, 8H, H-1 to H-6), 3.4 (s, 3H, NCH_3), 1.9–1.0 (M, 18H), 0.9 (distorted t, 9H, $Sn(CH_2)_3CH_3$); ^{13}C NMR ($CDCl_3$) δ 199.8 (C=S), 73.3, 71.9, 71.6, and 70.3 (C-2, C-3, C-4, and C-5), 63.8 (C-6), 60.2 (C-1), 45.4 (NCH_3), 28.7 (J_{CSn} = 20 Hz, CH_2CH_2Sn), 26.9 (J_{CSn} = 66 Hz, $CH_2(CH_2)_2Sn$), 17.4 (J_{CSn} = 348 Hz, CH_2Sn), 13.6 (CH_3). Anal. Calcd for $C_{20}H_{43}NO_5S_2Sn$: C, 42.90; H, 7.74; N, 2.50. Found: C, 42.83; H, 8.09; N, 2.27.

Tributyltin [5-[[(tributyltin)oxy]carbonyl]pentyl]dithiocarbamate (10): oil, 90%; ^1H-NMR ($CDCl_3$) 7.85 (m, 1H, NH), 3.4 (q, J = 6.6 Hz, 2H, CH_2N), 2.2 (t, J = 7.1, 2H), CH_2CO), 1.7–1.0 (M, 36H), 0.8 (t, J = 7.7 Hz, 18H, $Sn(CH_2)_3CH_3$); ^{13}C-NMR ($CDCl_3$) δ 199.8 (C=S), 178.5 (C=O), 48.5 (CH_2N), 34.3 (CH_2CO), 28.6, 28.4, 27.8, 27.6, 26.8, 26.3, 25.1, 16.9, and 16.2 (other CH_2), 13.5 (CH_3). (J_{CSn} cannot be determined due to overcrowding in the region of interest). Anal. Calcd for $C_{31}H_{65}NO_2S_2Sn_2$: C, 47.41; H, 8.34; N, 1.78. Found: C, 47.20; H, 8.28; N, 1.65.

Cleavage to the Dithiocarbamate Salts. To a solution of the stannylated derivative in methanol (3 mL/mmol) at 4 °C was added sodium hydrogen sulfide[31] (1 equiv per stannyl group), and the reaction mixture was stirred overnight. After concentration of the reaction mixture to one-third of its initial volume, dichloromethane and water were added and the resulting layers were partitioned. They contained, respectively, bis(tributyltin) sulfide and the desired dithiocarbamates; **11–17** were thus

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(26) Gleu, K.; Schwab, R. *Angew. Chem.* **1950**, *13*, 320–324.
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(31) Freshly prepared NaSH was used.[32] This MeOH/H_2O solution could be stored 1 week at 4 °C.
(32) Hodgson, H. H.; Ward, E. R. *J. Chem. Soc.* **1948**, 242.

obtained as the sole compounds after evaporation *without heating* of the volatiles under reduced pressure:

Sodium diethyldithiocarbamate (11): mp 97–99 °C;[25] ^{1}H-NMR (D_2O) δ 4.15 (q, J = 7.1 Hz, 4H, CH_2), 1.25 (t, J = 7.1 Hz, 6H, CH_3); ^{13}C-NMR (D_2O) δ 205.3 (C=S), 48.8 (CH_2), 11.4 (CH_3).

Sodium 1,4-butanediyldithiocarbamate (12):[26] mp 254 °C dec; ^{1}H-NMR (D_2O) δ 3.8–3.6 (M, 4H, CH_2N), 2.0–1.9 (M, 4H, CH_2CH_2N); ^{13}C-NMR (D_2O) δ 202.4 (C=S), 55.0 (CH_2N), 25.6 (CH_2CH_2N).

Disodium (1,4-butanediyl)bis(dithiocarbamate) (13):[27] mp 139 °C dec; ^{1}H-NMR (D_2O) δ 3.8–3.5 (M, 4H, CH_2N), 1.9–1.6 (M, 4H, CH_2CH_2N); ^{13}C-NMR (D_2O) δ 209.6 (C=S), 47.9 (CH_2N), 25.5 (CH_2CH_2N).

Disodium xylylenebisdithiocarbamate (14): mp > 300 °C; ^{1}H-NMR (D_2O) δ 7.4–7.15 (M, 4H, aromatics), 4.7 (m, 4H, CH_2); ^{13}C-NMR (D_2O) δ 211.1 (C=S), 138.0 (C_{ipso}), 129.1, 126.1 and 125.9 (other aromatics), 51.2 (CH_2N). Anal. Calcd for $C_{10}H_{10}N_2Na_2S_4 \cdot 4H_2O$: C, 29.69; H, 4.48; N, 6.93. Found: C, 30.06; H, 4.52; N, 6.51.

Sodium bis(2-hydroxyethyl)dithiocarbamate (15): mp 150–151 °C (lit.[28] 154.5–155.5 °C); ^{1}H-NMR (D_2O) δ 4.3 (t, J = 6.8 Hz, 2H, CH_2N), 3.95 (distorted t, 2H, CH_2O); ^{13}C-NMR (D_2O δ 211.1 (C=S), 59.1, and 56.8 (CH_2).

Sodium *N*-methyl-(D-*gluco*-2,3,4,5,6-pentahydroxyhex-1-yl)dithiocarbamate (16):[29] mp 162–165 °C; $[\alpha]^{20}_D$ −14.0° (c = 1.58, H_2O); ^{1}H-NMR (D_2O) δ 4.6–3.6 (M, 8H, H-1 to H-6), 3.5 (s, 3H, NCH_3); ^{13}C-NMR (D_2O) δ 210.0 (C=S), 72.1, 71.0, 70.9, and 69.8 (C-2, C-3, C-4, and C-5), 62.8 (C-6), 58.8 (C-1), 44.6 (CH_3).

Disodium *N*-dithiocarboxy-6-aminohexanoate (17): mp 214 °C (softens)–236 °C (fully melts); ^{1}H-NMR (D_2O) δ 3.45 (t, J = 6.4 Hz, 2H, CH_2N), 2.15 (t, J = 7.3 Hz, 2H, CH_2O), 1.7–1.15 (M, 6H); ^{13}C-NMR (D_2O) δ 209.5 (C=S), 184.0 (C=O), 48.1 (CH_2N), 37.6 (CH_2CO), 27.6, 26.2 and 25.7 (CH_2). Anal. Calcd for $C_7H_{11}NNa_2O_2S_2 \cdot 3H_2O$: C, 27.53; H, 5.61; N, 4.58. Found: C, 27.44; H, 5.72; N, 4.34.

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