of eluant in the filter flask. The process is analogous to continuous or extended elution TLC. The column in a horizontal position is sampled as above with a syringe.

Example. A 0.75-g mixture of steroids consisting of equal parts of 3β-hydroxy-5α-androstan-17-one, testosterone propionate, and pregnenolone acetate deposited on 4 g of Celite was added to a 100-g column of silica gel (E. Merck, 0.063–0.200 mm) that had been deactivated by the addition of 5% v/w of water and further equilibrated with 10% v/w of a solvent mixture of 30% ethyl acetate in hexane. The silica gel was contained in a nylon tube with a total length of 45 in. and a 2-in. circumference. The length of the silica gel column after packing with the aid of a vibrator was 39 in. The column was eluted with 125 mL of 30% ethyl acetate in hexane by using a vacuum of 100 mmHg in a period 12 min. A 100-μL syringe was used to puncture the nylon column, withdraw 5-μL samples, and spot them on a 10 × 20 cm TLC plate. Upon development with 30% ethyl acetate–hexene, the 3β-hydroxy-5α-androstan-17-one was found in the 2–6-in. region, the testosterone propionate was found in the 9–15-in. region, and the pregnenolone acetate was found in the 16–22-in. region. The 2–6-in. section gave 0.233 g of 3β-hydroxy-5α-androstan-17-one, mp 175–178 °C (lit.[7] mp 177–179 °C), the 9–15-in. section gave 0.238 g of testosterone propionate, mp 119–124 °C (lit.[8] mp 118–122 °C), and the 16–22 in. section gave 0.230 g of pregnenolone acetate, mp 148–149 °C (lit.[8] mp 149–151 °C).

Acknowledgment. Financial support by National Institutes of Health Grant GM 10421 is greatly acknowledged. Special thanks are due Dennis Faler.

Registry No. 3β-Hydroxy-5α-androstan-17-one, 481-29-8; testosterone propionate, 57-85-2; pregnenolone acetate, 1778-02-5.

(7) "Elsevier's"; Elsevier: New York, 1940; Vol. 14, p 144.
(8) "Merck Index", 9th ed.; Merck & Co.: Rahway, NJ, 1976.

Facile Conversion of Primary Thioamides into Nitriles with Butyltin Oxides[1]

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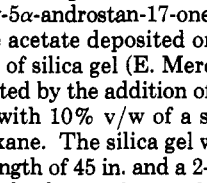
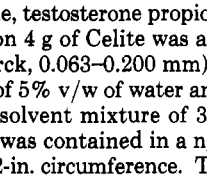
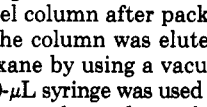
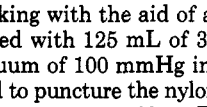
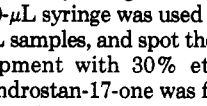
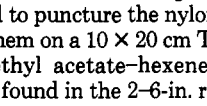
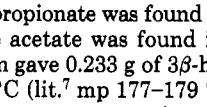
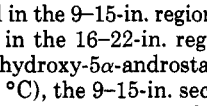
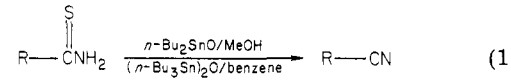
Butyltin oxides have recently received much attention for their utility as stereoselective nucleophile activators[2] and for mediating macrolide formation via template-driven processes.[3] During an investigation of the potential utilization of stannylation to enhance the nucleophilicity of heteroatoms bound to C-nucleosides, we observed that 3-amino-4-(2′,3′-di-*O*-isopropylidene-5′-*O*-trityl-β-D-ribofuranosyl)-2-thiocarboxamido-1*H*-pyrrole (1, Table I) was readily converted into the corresponding 2-cyanopyrrole[4] in the presence of dibutyltin oxide or bis(tri-*n*-butyltin) oxide under mild conditions in excellent yields (eq 1).

Table I

Entry No.	Thioamide	Product	Yield (%) by Method A	Yield (%) by Method B
1			98[a]	95[a]
2			100[a]	98[b]
3			91[a]	93[b]
4			62[a]	92[a]
5	C_6H_5-C(=S)-NH_2	C_6H_5CN	80[a]	88[c]
6	p-$O_2NC_6H_4CH_2$-C(=S)-NH_2	p-$O_2NC_6H_4CH_2CN$	55[a]	94[b]
7	$CH_3(CH_2)_{10}$-C(=S)-NH_2	$CH_3(CH_2)_{10}CN$	46[c]	77[c]
8	C_6H_5NH-C(=S)-NHC_6H_5	C_6H_5NH-C(=O)-NHC_6H_5	-	80[d]

[a] Isolated by preparative TLC. [b] The products were obtained by crystallization after addition of petroleum ether (bp 30–60 °C) to the residue. [c] Isolated by distillation. [d] Reaction time was 2 h. The product was isolated by direct crystallization from the reaction mixture.

Because of its general applicability, the procedure conveniently complements other methods presently available for such conversions.



$$R\text{—}C(=S)NH_2 \xrightarrow[(n\text{-}Bu_3Sn)_2O/\text{benzene}]{n\text{-}Bu_2SnO/MeOH} R\text{—}CN \qquad (1)$$

Dehydrosulfurization of thio amides and dehydration of amides into nitriles have been carried out with $Ph_3P/CCl_4/Et_3N$;[5] dichlorocarbene generated in a phase-transfer system containing $CHCl_3/NaOH/PhCH_2N^+Et_3Cl^-$;[6] $P(NEt_2)_3$ in boiling THF[7]; and, finally, with P_2O_5.[8] Several recently reported procedures that have been applied specifically to the conversion of thio amides into nitriles include metal ion promoted dehydrosulfurization;[9] treatment with PhC≡CC=NPh(NHPh);[10] EtOOCN=NCOOEt/Ph_3P/THF;[11] α-halogenated ketones, esters, or nitriles in DMF/NaOEt;[12] and Ph_3SnN=C=$NSnPh_3$.[13]

Our original observation (1, Table I) which utilized a slight molar excess of dibutyltin oxide in boiling methanol was found to be readily applicable to the conversion of

(1) This investigation was supported by funds from the National Cancer Institute, DHEW (Grants CA-08745, 18856, and 24634).
(2) D. Wagner, J. P. H. Verheyden, and J. G. Moffatt, *J. Org. Chem.*, **39**, 24 (1974); C. Auge, S. David, and A. Veyrieres, *J. Chem. Soc., Chem. Commun.*, 375 (1976); M. A. Nashed and L. Anderson, *Carbohydr. Res.* **56**, 419 (1977); M. A. Nashed, *ibid*, **60**, 200 (1978); R. M. Munavu and H. H. Szmant, *J. Org. Chem.*, **41**, 1832 (1976); T. Ogawa and M. Matsui, *Carbohydr. Res.*, **56**, C1 (1977); T.-L. Su, R. S. Klein, and J. J. Fox, *J. Org. Chem.*, **47**, 1506 (1982).
(3) A. Shanzer, J. Libman, and F. Frolow, *J. Am. Chem. Soc.*, **103**, 7339 (1981). K. Stelion, A. Szczygielska-Nowosielska, A. Fabre, M. A. Poupart, and S. Hanessian, *J. Am. Chem. Soc.*, **102**, 7578 (1980).
(4) M.-I. Lim and R. S. Klein, *Tetrahedron Lett.*, **22**, 25 (1981).
(5) R. Appel, R. Kleinstuck, and K.-D. Ziehn, *Chem. Ber.*, 1030 (1971).
(6) T. Saraie, T. Ishiguro, K. Kawashima, and K. Morita, *Tetrahedron Lett.*, 2121 (1973).
(7) T. Sodeyama, M. Kodomari, and K. Itabashi, *Chem. Lett.*, 577 (1973).
(8) L. Henry, *Ber. Dtsch. Chem. Ges.*, *2*, 305 (1869).
(9) D. P. N. Satchell, *Chem. Soc. Rev.*, *6*, 345 (1977).
(10) H. Fujita, R. Endo, and K. Murayama, *Bull. Chem. Soc. Jpn.*, **45**, 1582 (1972).
(11) M. D. Dowle, *J. Chem. Soc., Chem. Commun.*, 220 (1977).
(12) (a) H. Sing and C. S. Gandhi, *Synth. Commun.*, *9*, 569 (1979). (b) Similar conversion to nitriles was observed during the S-alkylation of primary thio amides: (1) A. Yamazaki, I. Kumashiro, T. Takenishi, and M. Ikehara, *Chem. Pharm. Bull.*, **16**, 2172 (1968); (2) F.-L. Chung, R. A. Earl, and L. B. Townsend, *Tetrahedron Lett.*, **21**, 1599 (1980).
(13) E. J. Kupchik and H. E. Hanke, *J. Organometal. Chem.*, **97**, 39 (1975).

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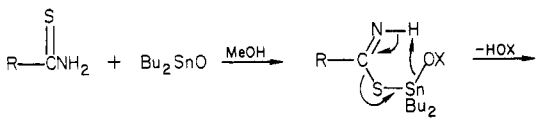
several aromatic (2–5) and aliphatic (6 and 7) thio amides into the corresponding nitriles. In all cases these conversions were completed within 30 min. Further studies indicated that bis(tri-*n*-butyltin) oxide, also a readily available organotin, is equally useful, if not superior. Thus, conversion of thio amides with 1.1 molar equiv of $(n\text{-}Bu_3Sn)_2O$ in boiling benzene under azeotropic conditions afforded the desired nitriles in very good to excellent yields in similarly short reaction times. These reactions appear to be specific for thio amides, since, under the same conditions, primary amides were unaffected by treatment with either butyltin oxide reagent.

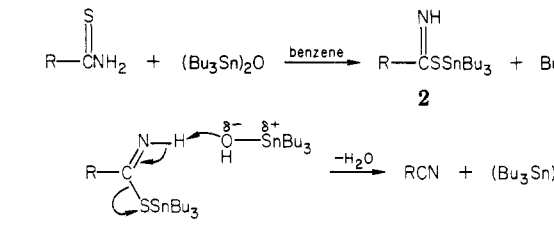
A plausible mechanism for the conversion of thio amides to nitriles with $n\text{-}Bu_2SnO$ in methanol is shown in eq 2 and



1, X = H or Me

RCN + Bu_2SnS (2)

involves nucleophilic attack by sulfur on the Sn=O function to give reactive intermediate **1**, where X = H. It is known, however, that dibutyltin oxide and methanol rapidly forms dibutyldimethoxytin.[14] It is therefore probable that attack by sulfur at the tin atom also involves this dimethoxytin derivative to give intermediate **1**, where X = Me. Either form of **1** can undergo a β elimination (presumably by the E_1 mechanism illustrated) to generate the nitrile with concomitant formation of dibutyltin sulfide. The possibility of an E_2 mechanism involving proton abstraction by methoxide ions formed by dissociation of dibutyldimethoxytin, however, cannot be precluded. The general mechanism offered is based on the isolation of dibutyltin sulfide as the only major byproduct of the reaction and on the reported ease with which thiols[14] and N-substituted thio amides[14c] undergo S-stannylation. An analogous mechanism for the dehydrosulfurization with bis(tri-*n*-butyltin) oxide is offered in eq 3 and involves



2 (3)

initial formation of sulfur–tin intermediate **2** and of tributyltin hydroxide. Subsequent β elimination would then afford the nitrile and bis(tri-*n*-butyltin) sulfide after water elimination.

Because of the usefulness of carbodiimides as versatile dehydrating reagents,[15] it was of interest to explore the possible application of the dehydrosulfurization reactions outlined above to the synthesis of carbodiimides from thioureas. Treatment of *N,N'*-diphenylthiourea with a slight excess of bis(tri-*n*-butyltin) oxide in benzene afforded instead the corresponding urea derivative (**8**, Table I) in good yields. The possibility that the diimide might have served as a transient intermediate in this conversion is under investigation.

The studies outlined above complement earlier reports on dehydrosulfurization of thio amide derivatives[5–13] and provide a simple and efficient procedure for the synthesis of nitriles from primary thio amides under mild, neutral conditions with readily available organotin reagents.

Experimental Section

The thio amides **1–3** were obtained from the corresponding nitriles[4,16] by treatment with hydrogen sulfide in pyridine and triethylamine.[17] The thio amides **4**, **5**, and **8** were commercially available. *p*-Nitrophenylthioacetamide (**6**) was obtained by treatment of *p*-nitrophenylacetonitrile with thioacetamide under acidic conditions.[18] Thiolauramide (**7**) was obtained from the reaction of lauramide with phosphorus pentasulfide in dioxane. Preparative TLC was performed on 500 μm silica gel GF plates (Analtech, Inc.).

General Procedure of Dehydrosulfurization (1–7). Method A. A mixture of the thio amide (1 mmol) and dibutyltin oxide (1.1 mmol) in methanol (8 mL) was heated to reflux for 30 min. For compound **7**, the reaction was carried out on a 10-mmol scale. After evaporation of the solvent, the product was isolated by the method specified in Table I and identified by comparison (^{1}H NMR, IR, and/or mp) with an authentic sample.

Method B. A mixture of the thio amide (1 mmol for **1–4** and **6**) and bis(tri-*n*-butyltin) oxide (1.1 mmol) in benzene (8 mL) was heated to reflux with azeotropic removal of water for 30 min. For compounds **5** and **7**, the reaction was carried out on a 10-mmole scal. Except for **8** (see Table I), the workup was identical with that described in method A.

Acknowledgment. We thank Marvin Olsen for recording the ^{1}H NMR spectra.

Registry No. 1, 83060-69-9; 2, 83060-70-2; 3, 83060-71-3; 4, 4621-66-3; 5, 2227-79-4; 6, 76254-70-1; 7, 56352-45-5; 8, 102-08-9; 1 nitrile, 77691-00-0; 2 nitrile, 83060-72-4; 3 nitrile, 83060-73-5; 4 nitrile, 100-54-9; 5 nitrile, 100-47-0; 6 nitrile, 555-21-5; 7 nitrile, 2437-25-4; *N,N'*-diphenylurea, 102-07-8; dibutyltin oxide, 818-08-6; bis(tri-*n*-butyltin) oxide, 56-35-9.

(14) See: (a) W. P. Neumann, "The Organic Chemistry of Tin", Interscience, New York, 1970; (b) R. C. Poller, "Chemistry of Organotin Compounds", Academic Press, New York, 1970; (c) A. K. Sawyer, "Organotin Compounds", Marcel Dekker, New York, 1971.

(15) (a) H. G. Khorana, *Chem. Rev.*, **53**, 145 (1953); (b) K. L. Agarwal, A. Yamazaki, and H. G. Khorana, *J. Am. Chem. Soc.*, **93**, 2754 (1971); (c) M. Mikolajczyk and P. Kielbasinski, *Tetrahedron* **37**, 233 (1981).

(16) The nitriles **2** and **3** were obtained by a general approach to 3-amino-2-cyanothiophenes recently developed in this laboratory. This method, which makes use of addition of an α-mercaptoacetonitrile derivative to 3-substituted cyanoacetylenes, followed by ring closure under basic conditions, will be reported elsewhere.

(17) A. Albert and C. J. Lin, *J. Chem. Soc., Perkin Trans. 1*, 210 (1977).

(18) E. C. Taylor and J. A. Zoltewicz, *J. Am. Chem. Soc.*, **82**, 2656 (1960).

(*E*)-3-(Trimethylsilyl)-2-propen-1-ol. An Improved Preparation

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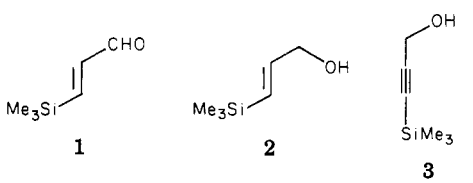
Received May 25, 1982

In connection with a research program on silicon-directed electrocyclic reactions[1] we required large quantities of (*E*)-3-(trimethylsilyl)propenal (**1**). This compound has



(1) Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2642.

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