Tetrahedron Letters,Vol.30,No.52,pp 7301-7304,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

SELECTIVE DESULFURIZATION OF 1,3-DITHIANES, -OXATHIOLANES AND -THIAZOLIDINES BY TRIBUTYLTIN HYDRIDE

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Abstract. *Selective desulfurization of 2-alkyl-1,3-dithianes, -oxathiolanes, or -thiazolidines* **1** *with one equivalent of tri-n-butyltin hydride yields acyclic compounds* $R^1R^2CHX(CH_2)_nSSnBu_3$ *(X = S,O,NH; n= 2,3),(2) which can be destannylated to the corresponding mercaptans* **3**.

γ-Alkylthiopropanethiols, and ß-alkoxy- and ß-alkylaminoethanethiols **3** are of interest as bidentate ligands, or as intermediates in the synthesis of other bi- or polydentate chelating ligands. We report the preparation of these by the selective cleavage of C-S bonds in 1,3-dithianes, -oxathiolanes, and -thiazolidines **1** (readily obtained from aldehydes or ketones and 1,3-propanedithiol, mercaptoethanol, or mercaptoethylamine) with tri-*n*-butyltin hydride (TBTH). The reduction of these heterocycles with one and two equivalents of TBTH[1] under a nitrogen atmosphere in refluxing benzene in the presence of 2,2'-azobis(isobutyronitrile) (AIBN) is outlined in **Scheme I**, and the results summarized in the **Table**. The reactions appear to involve the intermediacy of radicals, as they are initiated by AIBN and inhibited by hydroquinone or galvinoxyl.

The reduction of 1,3-dithianes **1a-f** (X=S) with one equivalent of TBTH resulted in the selective cleavage of only one of the geminal C-S bonds to produce the γ-alkylthiopropyl tributyltin sulfides **2** (X=S), with no overreduction to hydrocarbons **5** when the stoichiometry of dithiane to TBTH was controlled as 1:1. Destannylation of **2** to the corresponding γ-alkylthiopropyl mercaptans **3** was done in good yield by absorbing them on silica gel columns and slowly eluting with pentane/dichloromethane mixtures.[1a] Two equivalents of TBTH cleaved both geminal C-S bonds in dithianes **1** to give hydrocarbons **4** and 1,3-bis(tributylstannylthio)propane in good yield. The use of four equivalents of TBTH completely desulfurized dithianes, resulting in hydrocarbons **4** and bis(tributyltin) sulfide.

The reactions of 1,3-oxathiolanes **1g-k** (X=O) with TBTH[2] can be more complicated. The reaction of one equivalent of TBTH with heterocycles **1g, j, k** cleanly produced ß-alkoxyethyl tributyltin sulfides **2** (X=O) by the specific reduction of the C-S bond geminal to the C-O bond in the oxathiolanes. On the other hand, the product mixtures after reduction of **1h** and **1i** consisted of **2** and varying amounts of starting material and alkyl ethyl ethers **5**, the products of overreduction. We discovered no pattern in these reactions which might allow us to predict which oxathiolanes

Scheme I

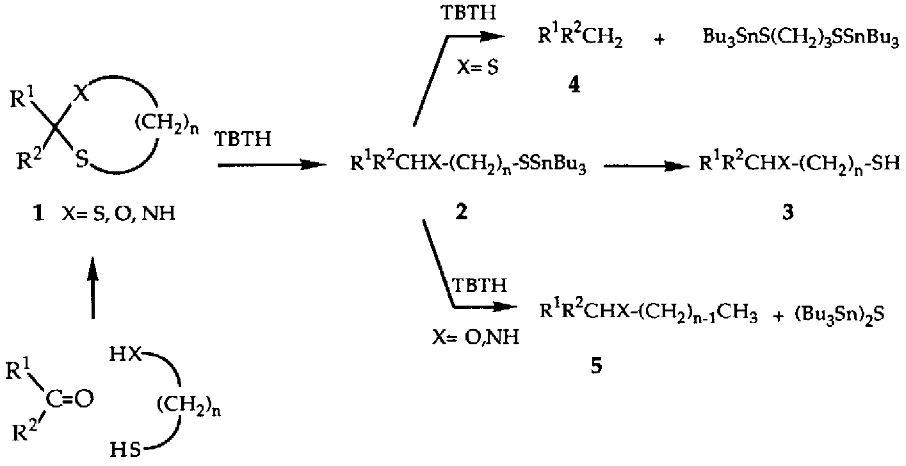


Table. **Reduction of 1,3-Dithianes, -Oxathiolanes, and -Thiazolidines with TBTH**

Heterocycles 1					Products of Reaction with TBTH (% yield):[a]									% Yield[c] Destannylation of 2 to 3[d]
					1 Equiv					2 Equiv				
	R^1	R^2	X	n	time (hr)	1	2	4	5	time (hr)	2	4	5	
1a	Ph	H	S	3	1.5	0	95	0	--	6	0	70	--	73
1b	CH$_3$	CH$_3$	S	3	1.2	0	89	0	--	7	0	--	--	78
1c	*n*-heptyl	H	S	3	7	0	96	0	--	5	0	52[b]	--	89
1d	-(CH$_2$)$_5$-		S	3	2	0	93	0	--	6	0	59[b]	--	82[e]
1e	2-furyl	H	S	3	15.5	0	87	0	--	19	0	--	--	60
1f	6-MeO-α-tetralyl		S	3	2.5	0	95	0	--	8	0	92	--	79
1g	Ph	H	O	2	3.5	0	92	--	0	40	75	--	25	80[f]
1h	CH$_3$	CH$_3$	O	2	4	0	60	--	20	40	25	--	75	52[f]
1i	*n*-heptyl	H	O	2	5	20	64	--	10	12	25	--	75	45[f]
1j	-(CH$_2$)$_5$-		O	2	5	0	90	--	0	31	40	--	60	78[f]
1k	2-furyl	H	O	2	60	0	85	--	0	100	80	--	20	65
1l	Ph	H	NH	2	20	0	99	--	0	--	--	--	--	67

[a] By NMR using diphenylmethane as internal standard. [b] By gas chromatographic analysis of reaction mixture using nonane as internal standard. [c] Isolated yields after column chromatography. [d] All new compunds exhibited NMR and IR spectra consistent with the assigned structures and analyzed for the appropriate molecular formula by either combustion or mass spectrometry. Several products 3 have been previously reported: [e] ref. 7. [f] ref. 8.

would cleanly reduce to **2**, and which would be complicated by overreduction to **5**. Under no circumstances did we observe the cleavage of a C-O bond.[3] The ß-alkoxyethyl tributyltin sulfides **2** were readily destannylated on silica gel columns to the ß-alkoxyethylthiols **3** (X=O). Formally, these procedures represent the alkylation of mercaptoethanol at oxygen, the less nucleophilic atom. The present work is complementary to the reduction of 1,3-oxathiolanes by $LiAlH_4/AlCl_3$ mixtures[4] and by borane reagents,[5] which result in the cleavage of C-O bonds to produce ß-alkylthioethyl alcohols.

When two equivalents of TBTH were reacted with 1,3-oxathiolanes **1g-k**, the product mixtures consisted of varying amounts of **2** (X=O) and the alkyl ethyl ethers **5**. The reduction of the primary C-S bonds in **2** is difficult under these reaction conditions, and we were unable to cleanly desulfurize these compounds to the ethyl ethers **5**, even after long reaction times. It appears that on prolonged heating, TBTH decomposes at a rate competitive with C-S cleavage. The use of more extreme conditions (> 6 equivalents of TBTH, and fresh AIBN, added over a period of up to 60 hrs) allowed for complete desulfurization.

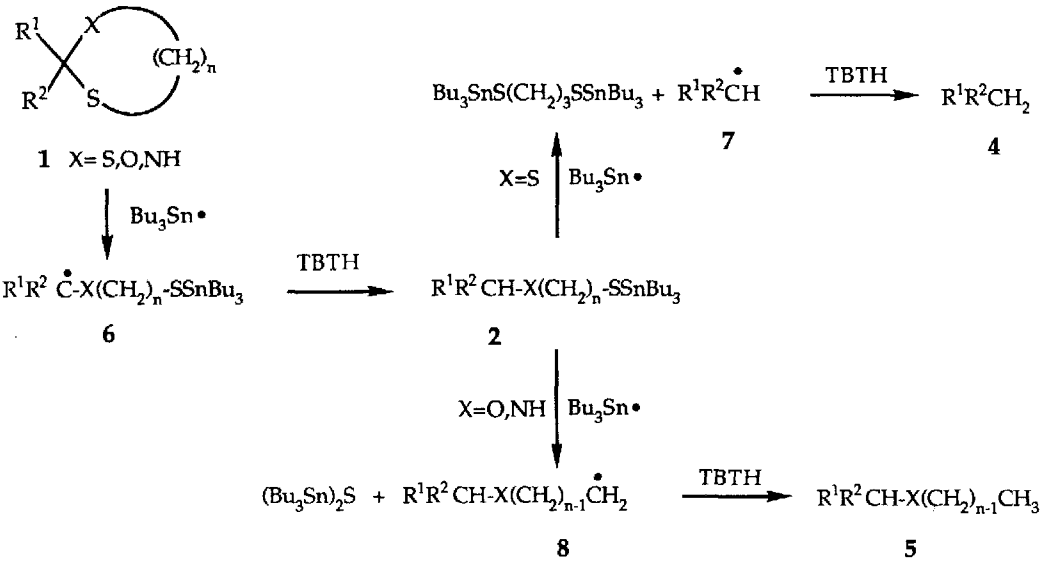
The reduction of 2-phenyl-1,3-thiazolidine (**11**) with one equivalent of TBTH[6] proceeds similarly to form the ß-benzylaminoethyl tributyltin sulfide **2** (X=NH, n=2). We were unable to effect destannylation to ß-benzylaminoethyl mercaptan on silica gel, yet this transformation was achieved with aqueous HCl.

The results from these reactions are consistent with the process outlined in **Scheme II**. Reaction of heterocycles **1** with tributylstannyl radical occurs at sulfur to produce carbon radical **6**. In those cases where X=S, this radical is stabilized by delocalization into adjacent empty d orbitals on sulfur. Hydrogen atom transfer from TBTH to **6** produces organotin sulfides **2**. Subsequent attack by additional equivalents of organotin radicals is also at sulfur. Where X=S reaction with tributylstannyl radical is at the sulfur in **2** leading to the more stable carbon radical **7** and 1,3-bis(tributylstannylthio)propane. Hydrogen atom transfer from TBTH to **7** produces hydrocarbons **4**. Where X=O or NH in intermediate **2**, reaction with $Bu_3Sn\cdot$ is also at sulfur, yet requires the intermediacy of primary carbon radicals **8**. The relative stabilities of the various carbon radical intermediates involved, and of the transition states leading to them, may explain the different reactivities of heterocycles **1** with TBTH, and the selectivity which this reagent exhibits towards the various C-S bonds in them.

The chemoselectivity of TBTH towards C-S bonds in these heterocycles was investigated by reacting equimolar mixtures of **1** and other compounds with various functionalities. Preliminary results indicate that the desulfurization of **1** to **2** is faster than reaction of TBTH with esters, aldehydes, ketones or alcohols. However organohalogen and -nitro compounds reduce faster than **1**.

The results of these TBTH reductions are reminiscent of the reduction of thioacetals,[7] thioketals,[7] and hemithioacetals[8] by alkali or alkaline earth metals in liquid ammonia or alkylamine solution. However, the present procedure offers advantages over dissolving metal reduction: (1) the simple experimental procedures; (2) very mild reaction conditions; (3) dissolving metal reduction is limited to 1,3-dithianes and -dithiolanes where neither R^1 nor R^2 is aryl, since the benzylic sulfide products **3** are desulfurized under those reaction conditions to the corresponding hydrocarbons **4**. With TBTH there is no such restriction (*cf* **Table** entries **1e-g**).

Scheme II



Acknowledgement. We thank the National Institutes of Health [MBRS-DRR S06 RR-081010] and the Research Corporation for support of this work.

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(Received in USA 15 August 1989)