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DISTANNOXANE-CATALYZED CLEAVAGE OF ACETALS AND SILYL ETHERS

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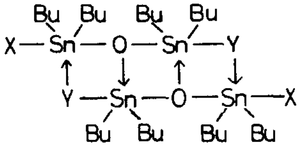
Summary: Deprotection of acetals including tetrahydropyranyl ethers and of silyl ethers can be achieved under neutral conditions by use of a distannoxane catalyst in excellent yields.

Protection of functional groups is an unavoidable process in organic synthesis.[1)] Hydroxy groups are conveniently protected as tetrahydropyranyl (THP) or silyl ethers whereas the most versatile masked form of carbonyl groups is acetals, which also are applied to protection of vic-diols. Regeneration of the parent functionalities from these masked forms is usually conducted under acidic conditions except for silyl ethers which can be removed by use of a fluoride ion.

Previously, we have disclosed the unique catalytic activities of 1,3-disubstituted tetrabutyldistannoxanes (**1**) for various types of functional group modifications, especially effective for oxygen-containing moieties.[2)] Here we wish to repert a new technique of removing the protection of alcohols, vic-diols, and carbonyl compounds. The potential synthetic utilities will be shown on the basis of the high chemoselectivity of the present method.

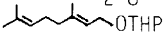
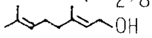
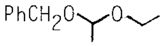


1a X = NCS,Y = NCS; **1b** X = Cl,Y = Cl; **1c** X = Br,Y = Br; **1d** X = NCS,Y = OH; **1e** X = Cl,Y = OH

Deprotection of THP ethers. Deprotection of THP ethers is usually performed with an acid catalyst[1)] and efforts have been made to conduct the reaction under milder conditions. Now, we have found that distannoxanes **1** are effective for the transformation of THP ethers into parent alcohols under neutral conditions.

The reaction was conducted simply by treating THP ethers with 1 mol% of **1**[3)] in methanol or THF-H_2O (50:1) at room temperature or at reflux. As shown in Table 1, the marked effect of the substituents, X and Y, has been observed: the 1,3-diisothiocyanato derivative **1a** exhibited the activity distinctly superior to other distannoxanes (entries 1-8). The mild reaction conditions enabled the deprotection of THP compounds carrying acid-sensitive moieties such as t-butyldimethylsiloxy (TBDMS), and geranyl groups (entries 11-12). Methoxymethyl (MOM) and methylthiomethyl (MTM) ethers remained intact. Exposure of one of these ethers in the presence of hexyl THP ether toward the present catalysis resulted in complete recovery of the former ether while the THP ether was quantitatively cleaved (entries 13-14). Since 1-ethoxyethyl ether could be deprotected under the same conditions (entry 15), 1 apparently recognized the difference between α-substituted-α-alkoxyethers and unsubstituted analogs.

Table 1. Deprotection of Tetrahydropyranyl Ethers

entry	ROTHP	Cat.	Reaction[a] Temp	Time, h	ROH	Yield, %
1	OctOTHP	**1a**	rfl	2	OctOH	97[b)]
2			rt	20		93[b)]
3		**1b**	rfl	16		90[b)]
4		**1c**	rfl	16		95[b)]
5		**1d**	rfl	16		86[b)]
6		**1e**	rfl	16		77[b)]
7		**1a**	rfl[c)]	23		93[b)]
8			rt[c)]	45		92[b)]
9	HexOTHP		rfl	2	HexOH	93[d)]
10	cyclo-HexOTHP		rfl	2	cyclo-HexOH	93[d)]
11	TBDMSO$(CH_2)_8$OTHP		rt	29	TBDMSO$(CH_2)_8$OH	89[e)]
12			rfl	12		88[b)]
13	HexOTHP + OctOMOM		rfl	2	HexOH	95[d,f)]
14	HexOTHP + OctOMTM		rfl	2	HexOH	93[d,g)]
15			rfl	14	$PhCH_2OH$	67[b)]

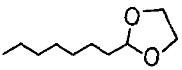
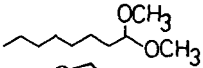
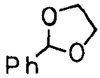
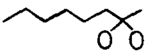
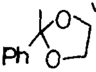
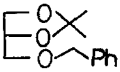
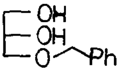
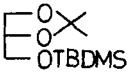
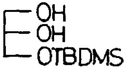
a) Methanol was employed as a solvent unless otherwise noted. b) Isolated yield by distillation. c) Solvent: THF-H_2O (50:1) d) Determined on the basis of GLC analysis. e) Isolated yield after column chromatography on silica gel. f) OctOMOM was recovered quantitatively. g) OctOMTM was recovered quantitatively.

Deprotection of Acetals. Regeneration of carbonyl compounds from acetals is usually conducted under acidic conditions.[1)] Thus, milder methods are highly desirable which, in particular, allow for efficient deprotection even in the coexistence of acid-sensitive functional groups.[4)] We have found that **1a**[5)] is quite useful for this purpose.

The reaction is conducted simply by heating acetals in the presence of **1a** (1 mol%) at 100 °C in diethylene glycol dimethyl ether (Diglyme)-water (2:1) or dioxane-water (2:1). The results are summarized in Table 2. Aliphatic and aromatic aldehydes as well as ketones are obtained in excellent yields (entries 1-5). Deprotection of acetonides gives vic-diols.

Since a benzyloxy group remained unchanged, the monobenzyl ether of glycerol was readily obtained (entry 6). As described later, the trimethylsilyl (TMS) ether of 2,3-O-isopropylideneglycerol was selectively desilylated under the similar conditions. In contrast, the TBDMS analog induced no desilylation but deacetalization preferentially (entry 7).

Table 2. Distannoxane-Catalyzed Deacetalization[a)]

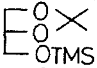
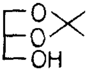
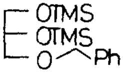
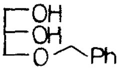
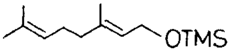
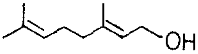
entry	Acetal	Reaction Time, h	Product	Yield, %
1		2	$\underline{n}$-$C_7H_{15}CHO$	87[b)]
2		2	$\underline{n}$-$C_7H_{15}CHO$	85[b)]
3		2	PhCHO	100[b)]
4		2	$\underline{n}$-$C_6H_{13}COCH_3$	93[b)]
5		2	$PhCOCH_3$	96[b)]
6		1		85[c)]
7		5		82[c)]

a) Reaction conditions: **1a** 0.01 mol% in Diglyme-water at 100 °C. Employment of a mixture of dioxane-water as a solvent gave the analogous results. b) Isolated yield by distillation. c) Determined on the basis of GLC.

Deprotection of Silyl Ethers. A TMS group is usually removed by heating in alcohols or by treatment with an acid or a fluoride ion at lower temperature.[1)] More stable TBDMS ethers are deprotected by use of a fluoride ion or under acidic conditions. Now **1a** has proved to serve as a good catalyst of desilylation as well.[5)]

As shown in Table 3, TMS ethers could be converted into the parent alcohols simply by treating with 1 mol% of **1a** in either methanol or THF-H_2O (5:1) at room temperature (entries 1-2). Under the analogous reaction conditions, TBDMS ethers resisted deprotection (entry 3). However, the cleavage proceeded smoothly in methanol at reflux (entry 4). Thus, the TMS group was removed selectively from a diol doubly protected by TMS and TBDMS groups (entry 5). Furthermore, a THP group remained intact in the presence of a TMS group which was deprotected (entry 6). As stated already, a THP group is removable under the analogous reaction conditions. Apparently, **1a** attacks the TMS protection in preference to the THP bond. Moreover, an acetal and a benzyloxy or geranyloxy group remained unchanged during the deprotection of a TMS group (entries 7-9).

Table 3. Deprotection of Silyl Ethers[a)]

entry	Silyl Ether	Reaction Temp	Time, h	ROH	Yield, %
1	OctOTMS	rt	17	OctOH	96[b)]
2		rt[c)]	14	OctOH	89[b)]
3	OctOTBDMS	rt	15		0
4		rfl	16	OctOH	70[b)]
5	TBDMSO$(CH_2)_6$OTMS	rt	48	TBDMSO$(CH_2)_6$OH	88[d)]
6	THPO$(CH_2)_6$OTMS	rt	11	THPO$(CH_2)_6$OH	92[d)]
7		rt	0.5		87[e)]
8		rt	1		90[e)]
9		rt	16		95[b)]

a) Reaction conditions: **1a** 1 mol%; methanol as a solvent unless otherwise noted. b) Isolated yield by distillation. c) Solvent: THF-H_2O (5:1). d) Isolated yield after column chromatography on silica gel. e) Determined on the basis of GLC.

In summary, distannoxanes have proved to be effective for cleavage of diverse protecting groups. The mild reaction conditions enables the selective deprotection among coexisting functional groups. The synthetic utility of the present method is apparent on these grounds as well as the facile availability of 1 from commercial Bu_2SnCl_2 and/or Bu_2SnO.[3)]

Acknowledgment. Thanks are due to T. Nagai, H. Nakayama, and K. Kosugi for their experimental work.

References

(1) T. W. Greene, "Protective Groups in Organic Synthesis", John Wiley and Sons, New York, N. Y., 1981. .

(2) J. Otera, T. Yano, A. Kawabata, and H. Nozaki, Tetrahedron Lett., **27**, 2383 (1986). J. Otera, T. Yano, Y. Himeno, and H. Nozaki, Ibid., in press.

(3) For the preparation of **1**, see T. Yano, K. Nakashima, J. Otera, and R. Okawara, Organometallics, **4**, 1501 (1985), and references cited therein.

(4) For the most recent study: K. S. Kim, Y. H. Song, B. H. Lee, and C. H. Hahn, J. Org. Chem., **51**, 404 (1986).

(5) Other distannoxanes also catalyzes the reaction but less effectively.

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