CASE STUDY

#CS_SM-001

Removal of Protecting Groups

SILICYCLE

A Practical Cleavage of Acetals Using Silia*MetS*® Thiol

Removing protecting groups from a synthesis pathway can prove difficult. In order to overcome this challenge, a method using Silia*MetS*® Thiol was developed for the deprotection of various aromatic and aliphatic acetals to their corresponding catechol or diol derivatives.

This interesting process has many advantages, including an overall simplified procedure compared to the traditional deprotection methods. To start it is a mild procedure, is amenable to scale-up, does not require inert atmosphere and can be carried out at ambient temperature. Both clean conversions and good chemoselectivity can be observed. The thiol stench was avoided, and it allows the use of solvent independent thermally stable reagents. In addition, this process allows the removal of toxic or difficult reagents and by-products by a simple filtration. Finally, in many cases, purification by chromatography was unnecessary which reduces the amount of solid waste while not impacting yields adversely.

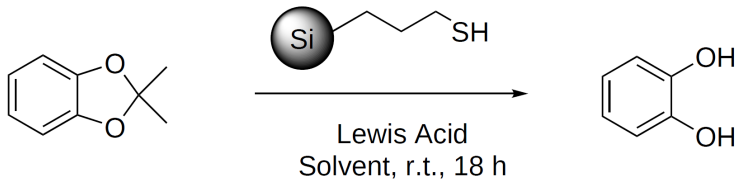

Table 1: Yields of Catechol 2 in different solvents and acids

Yields of Catechol 2 in different solvents and acids				
Entry	**Si-Thiol (equiv)**	**Lewis acid (equiv)**	**Solvent**	**Yield (%)**
1	1.0	$BF_3 \cdot Et_2O$ (2.0)	Dichloromethane	75
2	1.0	$BF_3 \cdot Et_2O$ (1.0)	Dichloromethane	88
3	5.0	$BF_3 \cdot Et_2O$ (1.0)	Dichloromethane	93
4	2.0	$BF_3 \cdot Et_2O$ (1.0)	Dichloromethane	>99
5	2.0	$FeCl_3$ (1.0)	Dichloromethane	99
6	2.0	$AlCl_3$ (1.0)	Dichloromethane	99
7	2.0	$ZnCl_2$ (1.0)	Dichloromethane	99
8	2.0	p-TsOH (1.0)	Dichloromethane	88
9	2.0	$BF_3 \cdot Et_2O$ (1.0)	Acetonitrile	>99
10	2.0	$BF_3 \cdot Et_2O$ (1.0)	Dichloromethane	90
11	2.0	$BF_3 \cdot Et_2O$ (1.0)	tert-Butyl methyl ether	90
12	2.0	$BF_3 \cdot Et_2O$ (1.0)	Diethyl ether	74
13	2.0	$BF_3 \cdot Et_2O$ (1.0)	Acetone	25
14	2.0	$BF_3 \cdot Et_2O$ (1.0)	N,N-Dimethyl-formamide	Mixture of products
15	2.0	$BF_3 \cdot Et_2O$ (1.0)	N,N-Dimethyl-acetamide	Mixture of products
16	2.0	$BF_3 \cdot Et_2O$ (1.0)	Methanol	No reaction

This method was also investigated by examination of an array of structurally diverse acetals and it gave promising results with good chemoselectivity being displayed.

De Léséleuc, M. et al. Eur. J. of Org. Chem., 2019, 44, 7389 - 7393
Prometic Biosciences Inc.

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https://www.silicycle.com/products/metal-scavengers/portfolio/r51030b