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A Facile Method for the Cleavage of Acetals by the Combined Use of Samarium Trichloride and Chlorotrimethylsilane

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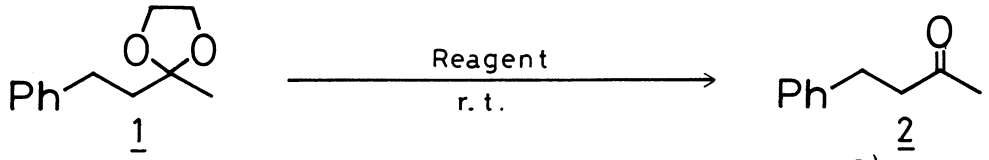
Cleavage of acetals by a stoichiometric or a catalytic amount of samarium trichloride and chlorotrimethylsilane in the absence of a proton source proceeded smoothly giving the corresponding carbonyl compounds in high yields.

The selection of a protective group is an important problem for the achievement of a multistep organic synthesis. Acetal is well-known as one of the most useful protective groups, which is stable under non-acidic conditions and can be cleaved in the presence of an acid.[1] In the case where there exist many acid-labile functional groups, selective cleavage of acetals is desired. To overcome the problem, several non-acidic cleaving methods of acetals have been employed. Although conversion of acetals to carbonyl compounds under non-aqueous conditions using iodotrimethylsilane (TMSI),[2a] trichloromethylsilane-sodium iodide,[2b] dimethylboron bromide,[2c] boron trifluoride-iodide ion,[2d] phosphorous triiodide,[2e] lithium tetrafluoroborate,[2f] or trityl perchlorate[2g] was reported, availability and yields were not sufficient. We wish to describe here a new method for the cleavage of acetals by the use of samarium trichloride and chlorotrimethylsilane (TMSCl) in the absence of a proton source under mild conditions.

Although the cleavage of dimethylacetals by TMSI has been known to give the corresponding carbonyl compounds in good yields, it was not useful in the case of 1,3-dioxolane.[2a] That is, 2-methyl-2-phenethyl-1,3-dioxolane (**1**) was treated with TMSI at room temperature to give 4-phenyl-2-butanone (**2**) in 41% yield (entry 1). On the other hand, the use of TMSCl which is more available and milder reagent afforded **2** only in 6% yield, and 85% of **1** was recovered. Samarium trichloride was found to be an efficient activator for the cleavage to furnish the ketone **2** in 99% yield (entry 3).[3] As a solvent, THF or CH_3CN was better than CH_2Cl_2 (entries 3-5). When samarium trichloride was employed without TMSCl, the reaction scarcely took place (entry 6). Samarium was superior to cerium and lanthanum (entries 7 and 8), and other Lewis acids, such as zinc chloride, stannous chloride, and ferric chloride, were found to be less effective (entries 9-11). These results were summarized in Table 1.

The present samarium trichloride-TMSCl reaction system was applied for various acetals. As shown in Table 2, ketones or aldehydes were obtained in high yield. Remarkable features of the present method were as follows: a) Conversion



1 2

Table 1. Transformation of 1 to 2 under various conditions[a)]

Entry	Reagent (equiv.)	Solvent	Reaction time/h	Yield[b)] of 2/%	Recovery[b)] of 1/%
1	TMSI (1.1)	CH_2Cl_2	1	41	-
2	TMSCl (1.1)	THF	93	6	85
3	$SmCl_3$ (1.1) + TMSCl (1.5)	THF	42	99	-
4	$SmCl_3$ (1.1) + TMSCl (1.7)	CH_3CN	63	91	9
5	$SmCl_3$ (1.5) + TMSCl (1.6)	CH_2Cl_2	64	34	64
6	$SmCl_3$ (1.1)	THF	50	6	82
7	$CeCl_3$ (1.1) + TMSCl (1.5)	THF	85	10	83
8	$LaCl_3$ (1.1) + TMSCl (1.5)	THF	67	12	82
9	$ZnCl_2$ (1.1) + TMSCl (1.5)	THF	50	6	89
10	$SnCl_2$ (1.1) + TMSCl (1.5)	THF	69	14	79
11	$FeCl_3$ (1.1) + TMSCl (1.1)	CH_2Cl_2	2	43	-

a) All reactions were performed on 1 mmol scale at room temperature. b) Isolated yield.

to the corresponding carbonyl compounds from dimethylacetals, diethylacetals, 1,3-dioxolanes and even a 1,3-dioxane was easily proceeded. b) The cleavage of acyclic acetals was faster than cyclic acetals. c) A catalytic amount (10 mol%) of samarium trichloride was enough to promote the cleavage of the dimethylacetals (Method B). d) Transformation of acetals to aldehydes was slower than that to ketones, and the conversion to an aliphatic aldehyde did not proceed completely (entries 10 - 12). Chemoselective transformation of the acetals to ketones was achieved by the treatment with diacetals of ketone and aldehyde (entries 13 and 14). e) Acid-labile functional groups, such as *t*-butyldimethylsilyl ether and methoxymethyl (MOM) ether, were tolerant under the reaction conditions (entries 15 and 16). f) Benzyl ether[2b,4a)] and methyl ester,[2b,4b)] which are known to be cleaved by using TMSI, trichloromethylsilane-sodium iodide, or dimethylboron bromide, were also stable (entries 17 - 19).

The mechanism of the cleavage might be almost the same as that in the case of TMSI as shown in Scheme 1.[2a)] Although active species is not ascertained, novel active species such as **4** may be involved because samarium trichloride became more dissolvable in THF by the addition of TMSCl.

The representative procedure for the cleavage of 2,2-dimethoxy-4-phenylbutane (**3**) is as follows: Samarium trichloride (619 mg, 2.41 mmol) was dried at 140 - 150 °C for 1 h *in vacuo* and stirred in THF (5 mL) at room temperature for 1 h.[5)] After addition of TMSCl (262 mg, 2.41 mmol) in THF (2 mL), the mixture was further stirred for 2 h. A solution of 2,2-dimethoxy-4-phenylbutane (**3**) (421 mg, 2.17

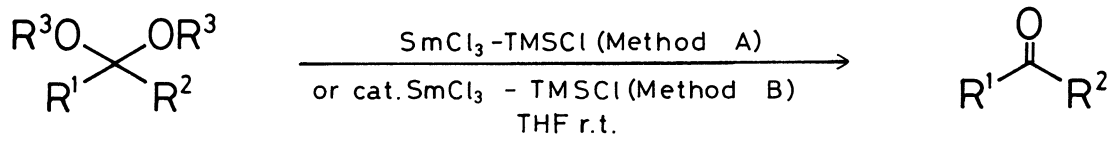
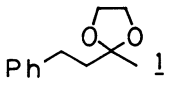
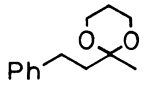
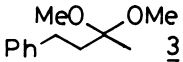
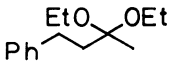
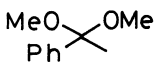
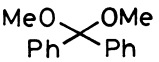
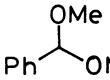
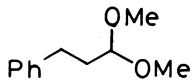
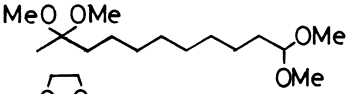
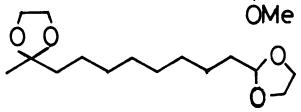
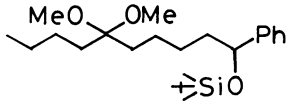
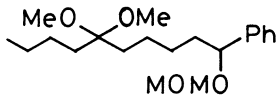
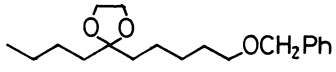
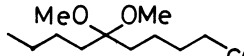
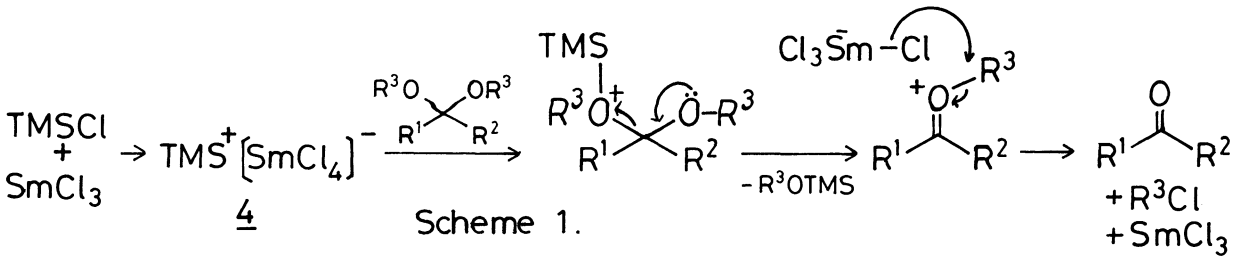


Table 2. Cleavage of Acetals by $SmCl_3$-TMSCl

Entry	Acetal	Method[a]	Reaction time	Isolated yield/%
1	 1	A	42 h	99
2		A	32 h	92
3	 3	A	3.5 h	93
4		B	29 h	89
5		A	3 h	91
6		A	3 h	79
7		B[b]	5 min	75
8		A	30 h	93
9		B	5 d	90
10		A	8 d	(>95)[c]
11		B	10 d	(94)[c]
12		A	6 d	47
13		A	10 min	71[d]
14		A	5 h	92[e]
15		A	45 min	93
16		A	35 min	92
17		A	68 h	97
18		A	5.5 h	94
19		B	28 h	92

a) Method A: 1.1 equiv. of $SmCl_3$ and 1.0 - 1.5 equiv. of TMSCl were used. Method B: 0.1 equiv. of $SmCl_3$ and 1.5 - 2.0 equiv. of TMSCl were used. b) Reaction temperature was 50 °C. c) Yield was determined by GLC (SE-30). d) 11,11-Dimethoxy-2-undecanone was the product. e) 2-(9-Oxodecanyl)-1,3-dioxolane was the product.



Scheme 1.

mmol) in THF (2 mL) was added to the suspension, and the reaction mixture was stirred for 3.5 h at room temperature. The reaction was quenched with sat. aqueous $NaHCO_3$, and the organic materials were extracted with CH_2Cl_2 and dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by TLC on silica gel to give 4-phenyl-2-butanone (2) (300 mg) in 93% yield.

By the use of the present samarium trichloride-TMSCl system,[6] the cleavage of acetals can be smoothly accomplished in the absence of a proton source without destruction of other functional groups.[7]

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