Reductive cleavage of the C–O bond of acetals and orthoesters: reduction by silane in the presence of a Rh–PPh$_3$ complex

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Reductions of acetals to ethers and of orthoester to acetal by hydrosilane using rhodium catalyst are described.

Cleavage of the C–O bond is one of the most important methods for the transformation of functional groups to other functionalities. Among catalytic reactions developed so far, the most successful example is the nucleophilic substitution of allyl acetate derivatives *via* the π-allyl-metal species.[1] Aryl triflates are used for the coupling reaction by Ni or Pd catalysts.[2] Yamamoto *et al.* reported several applications of the cleavage of the C–O bond in acid anhydrides by palladium complexes.[3] Nevertheless, for the non-activated C–O bond there is still room to utilize a catalytic application, although combinations of Lewis acid and/or reducing agent can reduce acetals and orthoesters.[4]

Silanes were recently demonstrated to be reductants combined with metal species, such as Ti,[5] Mn,[6] Rh[7] and Ru.[8] We have already developed the reduction of carboxylic acid derivatives, such as esters, carboxylic acids and amides, by silane in the presence of Rh complexes.[9] In the course of this study, we found that our reduction system can reduce the C–O bond in acetals and orthoesters.†

2-Phenyl-1,3-dioxane (**1a**) was allowed to react with phenylsilane in the presence of rhodium catalyst in THF. Dibenzyl was added as an internal standard after 48 h, and then the mixture was treated with 1 M NaOH. By ^{1}H NMR analysis of the concentrating organic layers, 3-benzyloxy-1-propanol (**2a**) was found to be the main product.
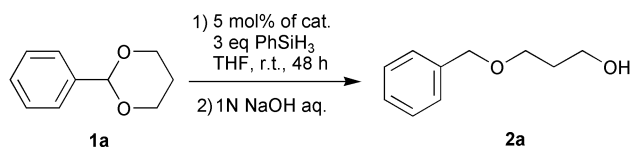
Among the catalysts examined, RhCl(PPh$_3$)$_3$ and [RhCl(cod)]$_2$–4PPh$_3$ showed high catalytic activities. These results are the same as the reduction of carboxylic acid derivatives by silane.[9] When several phosphines were tested to be combined with [RhCl(cod)]$_2$, PPh$_3$ resulted in the highest yield of product. Concerning the amount of catalyst, at least 2.5 mol% of RhCl(PPh$_3$)$_3$ was needed. For the examination of the kind of silane as a reductant, PhSiH$_3$ was the most effective; the yield of **2a** reached 98% for the reaction at 50 °C. For Ph$_2$SiH$_2$, which was effective for the reduction of carboxylic acid derivatives, reduction proceeded in low yield. Three equivalents of silane to substrate had to be used for this reaction, and 2 equivalents of PhSiH$_3$ resulted in a lower yield of **2a**.

Cyclic and dimethyl acetals were employed for this reduction (Table 1). Substituents on 1,3-dioxane and 1,3-dioxolane influenced the reactivity. The substituent on C2 was particularly necessary for reduction to occur. Substrates having an aryl substituent on C2 were smoothly reduced to hydroxy ethers, while a benzyl substituent on C2 (**1b**, entry 2) decreased the yield. Acetophenone acetals **1c** and **1d**, which have two substituents on the C2 of 1,3-dioxane or 1,3-dioxolane, were also reduced smoothly (entries 3 and 4). Benzaldehyde dimethyl acetal derivative **1g** was also reduced by this reduction system (entry 7).
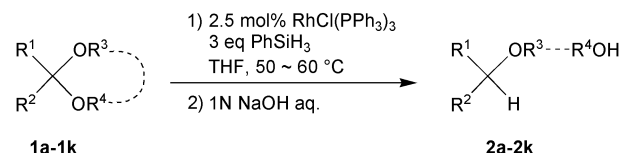

Table 1 Reduction of various acetals by PhSiH$_3$ in the presence of RhCl(PPh$_3$)

| Entry	Acetals		Recovered 1 (%)[b]	Yield of 2 (%)[b]
1		**1a**	8	91
2[c,d]		**1b**	29	66
3		**1c**	11	89
4		**1d**	15	81
5		**1e**	31	64
6[c,e]		**1f**	11	86
7[c]		**1g**	18	77

[a] A mixture of RhCl(PPh$_3$)$_3$ (0.0125 mmol), PhSiH$_3$ (1.5 mmol), acetal (0.5 mmol) in THF (1.0 mL) was stirred. [b] Determined by ^{1}H NMR based on starting material **1**. [c] 60 °C. [d] 72 h. [e] Four eq. of PhSiH$_3$ was used.

Having successfully reduced acetals using our reducing system, we applied this catalysis for the reaction of orthoesters. An orthoester is considered to be converted to the acetal and then to the ether, sequentially. If the reduction of an orthoester could stop at the acetal stage, an aldehyde would be obtained by the reduction of an ester *via* the orthoester and acetal (Scheme 1).

Trimethyl orthobenzoate (**3**) was used as an orthoester. RhH(CO)(PPh$_3$)$_3$ and RhCl(PPh$_3$)$_3$ showed good conversions with low selectivity for **4**. PhSiH$_3$ showed the best activity as a
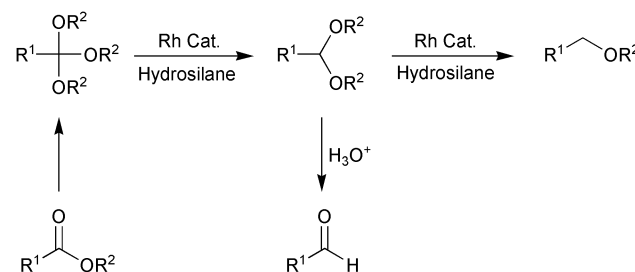
Scheme 1 Reduction of orthoester.
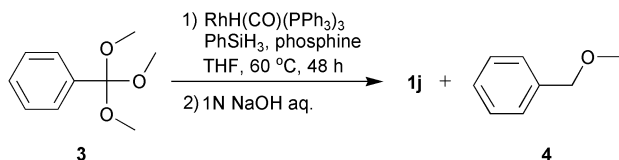
reductant. In order to getting high selectivity for **4**, the highest active catalyst RhH(CO)(PPh₃)₃ was used, and several reaction conditions were changed. When the amount of catalyst was decreased to 2.0 mol% from 5.0 mol%, conversion was not changed but the yield of **4** increased to 79% from 20%. Finally, effect of the addition of phosphines for this reduction was investigated (Table 2).

Table 2 The effect of additional phosphines on the reduction of trimethyl orthobenzoate (**3**)

Entry	Phosphine–**3** (mol%)	Conv. (%)^b	**1j** (%)^b	**4** (%)^b
1	None	68	59	7
2	PPh₃ (10)	87	80	7
3	P(4-C₆H₄F)₃ (10)	81	70	8
4	P(4-C₆H₄OMe)₃ (10)	100	91^c	9
6^d	P(4-C₆H₄OMe)₃ (5)	99	93	7
7^{d,e}	None	34	29	4

^{a} A mixture of RhH(CO)(PPh₃)₃ (0.005 mmol), PhSiH₃ (1.50 mmol), phosphine (0.025–0.100 mmol), trimethyl orthobenzoate (**3**) (0.5 mmol) in THF (1.0 mL) was stirred at 60 °C for 48 h. ^{b} Determined by ¹H NMR. ^{c} Contains benzaldehyde (4%). ^{d} RhH(CO)(PPh₃)₃ (0.0025 mmol) was used. ^{e} 96 h.

Adding 10 mol% of PPh₃ to the reaction of **3** with 3 eq. of PhSiH₃ in the presence of 1 mol% of RhH(CO)(PPh₃)₃ at 60 °C for 48 h increased the conversion of **3** by 19% with a 21% increase of **4** compared with no additive. Then various phosphines were tested as an additive for this reaction. Addition of P(4-CH₃OC₆H₄)₃ showed better result than PPh₃ and P(4-C₆H₄F)₃, while addition of other monophosphines (PMePh₂, P(o-Tol)₃) and bidentate phosphines (dppe, dppb, BINAP) resulted in lower conversions. Using 0.5 mol% of RhH(CO)(PPh₃)₃ with 5 mol% of this phosphine resulted in almost quantitative conversion with 93% of **4** and 7% of **5** formed. This illustrates the dramatic effect of adding phosphine compared with no addition of phosphine (only 34% conversion for twice as long reaction time). Although the reason is not clear yet, addition of phosphine may accelerate the reductive elimination step in the catalytic cycle.

The rhodium–silane reduction system is effective for the reductive cleavage of sp³-carbon sp³-oxygen bonds. Acetals were reduced to ethers in up to 98% yield using PhSiH₃ in the presence of RhCl(PPh₃)₃. On the other hand, trimethyl orthobenzoate was reduced to benzaldehyde dimethyl acetal in 93% yield by the same silane in the presence of 0.5 mol% of RhH(CO)(PPh₃)₃ and 5 mol% of P(4-CH₃OC₆H₄)₃. This is the first example of homogenous catalytic reduction of acetals and orthoesters using hydrosilane as a reducing reagent in the presence of a rhodium complex. Consequently, the method in this report is thought to be a new route for the synthesis of ethers, acetals and aldehydes under mild conditions.

Notes and references

† Typical procedure for reduction of acetals by phenylsilane in the presence of RhCl(PPh₃)₃: in a 20 mL Schlenk tube was dissolved RhCl(PPh₃)₃ (23 mg, 0.025 mmol) in THF (1 mL). To this solution were added 2-phenyl-1,3-dioxane (**1**) (0.5 mmol) and PhSiH₃ (**2**) (0.19 mL, 1.5 mmol), and the solution was stirred at room temperature for 48 h. Dibenzyl (91 mg, 0.5 mmol, as an internal standard), THF (5 mL), and 1 M NaOH aq. (5 mL) were added, and the mixture was stirred for 2 h. A mixture of the products and dibenzyl was obtained by extraction with diethyl ether followed by concentration. The yield was determined by ¹H NMR spectroscopic analysis using an internal standard method.

Procedure for reduction of trimethyl orthobenzoate (**3**) by RhH(CO)(PPh₃)₃ in the presence of P(4-CH₃OC₆H₄)₃: in to a 20- mL Schrenk tube were added RhH(CO)(PPh₃)₃ (0.005 mmol), phosphine (0.025 mmol), trimethyl orthobenzoate (**3**) (0.5 mmol), and THF (1.0 mL). Then, to this mixture were added dibenzyl (91 mg, 0.5 mmol) and PhSiH₃ (1.5 mmol), and the mixture was stirred at 60 °C for 24 h. After the reaction, THF (5 mL) and 1 M NaOH aq. (5 mL) were added, and the mixture was stirred for 2 h. The mixture was extracted, and the organic layer was dried over Na₂SO₄ followed by concentration to give crude product. This mixture was analyzed by ¹H NMR measurement.

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