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Homogeneous Catalysis

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Efficient Reduction of Esters to Aldehydes through Iridium-Catalyzed Hydrosilylation**

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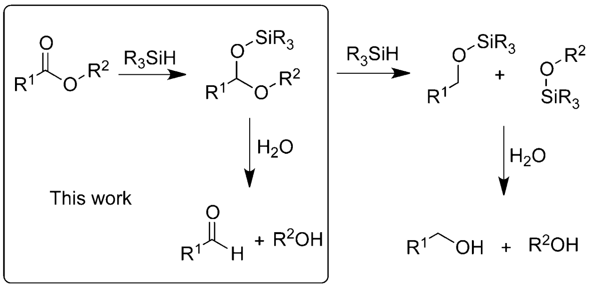
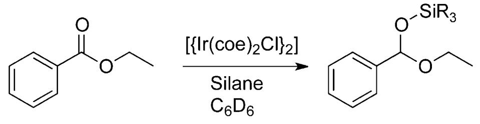
Reduction of esters to aldehydes is challenging since the aldehyde products are often more reactive toward nucleophilic hydride reducing agents than the starting esters.[1] Hence, bulky reducing agents such as diisobutylaluminum hydride (DIBALH) or lithium tri-*tert*-butoxyaluminum hydride have been developed for this transformation.[2] However, these reagents are usually toxic, air- and moisture-sensitive, require exigent reaction conditions, and are not compatible with many functional groups. In addition, even these reagents often result in over-reduction of substrates. Alternatively, reduction of carbonyl derivatives can be achieved through catalytic hydrosilylation followed by hydrolysis of the silyl group.[3] For example, hydrosilylation of ketones and aldehydes followed by acidic or basic workup affords secondary and primary alcohols.[3e,f] This strategy has also been widely applied to the reduction of esters to alcohols or ethers (Scheme 1).[4] In contrast, there have been very few examples of controlled reduction of esters to silyl acetals, which upon hydrolysis give aldehydes.[5] One such example employed a ruthenium carbonyl complex at high temperature (100 °C) and demonstrated limited substrate scope.[5a] Another method requires using 2-pyridinyl esters as substrate and cannot be applied to "simple" esters.[5b] Finally, $B(C_6F_5)_3$ has been used to catalyze reduction of esters to silyl acetals with Ph_3SiH, although the reactions were accompanied with substantial over-reduction to silyl ethers and alkanes.[5c] Here we report a simple and highly efficient method for reduction of esters to aldehydes via silyl acetal intermediates generated by iridium-catalyzed hydrosilylation. The catalyst, $[\{Ir(coe)_2Cl\}_2]$, (coe = cyclooctene) can be easily prepared and is commercially available, and this reduction system exhibits high conversion at low catalyst loading (down to 0.1 mol %) and good functional group compatibility.



Scheme 1. Reduction of esters through catalytic hydrosilylation.

Previously we showed that the binuclear iridium complex $[\{Ir(coe)_2Cl\}_2]$ is an efficient catalyst for reduction of secondary amides to secondary amines through hydrosilylation using diethylsilane.[6] For reduction of ethyl benzoate we screened several silanes, including diethylsilane, in C_6D_6 at room temperature (Table 1). Consistent with previous results concerning amide reduction, diethylsilane proved most effective, and hydrosilylation of the carbonyl double bond took place rapidly at room temperature to afford the diethylsilyl acetal (Table 1, entry 1). Several tertiary silanes screened proved to be ineffective (Table 1, entries 2–6), whereas bulkier secondary silanes react more slowly than diethylsilane (entries 7 and 8).

Table 1: Screening experiment for hydrosilylation of esters.[a]



1a **2a**

Entry	Silane	*t* [h]	Conversion [%]
1	Et_2SiH_2	2	> 99
2	Et_3SiH	12	0
3	TMDS[b]	12	0
4	PMHS[c]	12	0
5	$EtMe_2SiH$	12	0
6	$(EtO)_3SiH$	12	0
7	Ph_2SiH_2	24	23
8	$PhMeSiH_2$	5	96

[a] Reaction conditions: ethyl benzoate (0.1 mmol) with $[\{Ir(coe)_2Cl\}_2]$ (0.15 μmol) and silane (1.5 equiv) in C_6D_6 (0.35 mL). Reactions were run at room temperature. Conversions were determined by ^1H NMR spectroscopy. [b] 1,1,3,3-Tetramethyldisiloxane (1.5 equiv, 3 equiv SiH functionality). [c] Polymethylhydrosiloxane (5 equiv), assuming MW = 60 for each SiH functionality.

In ester reductions studied here, cleavage of the C–O bond of the acetal intermediates by diethylsilane to give silyl ethers occurs much more slowly than the initial hydrosilylation and generally requires higher temperatures.[7] Hence,

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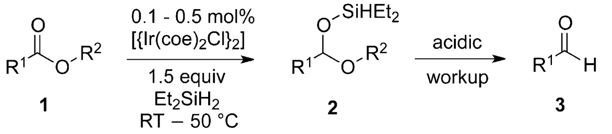
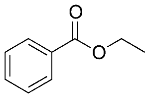
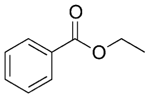
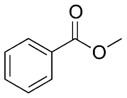
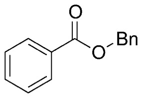
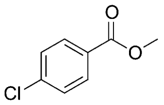
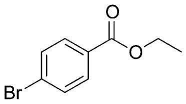
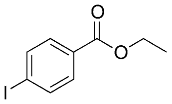
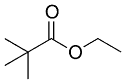
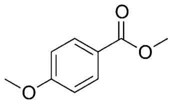
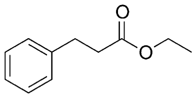
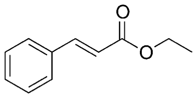
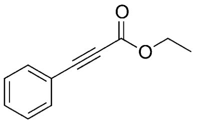
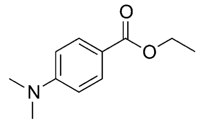
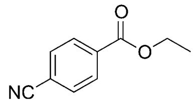
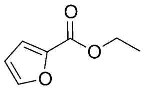
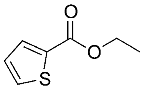
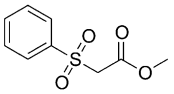
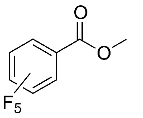
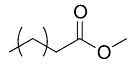
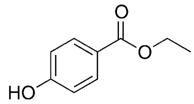
optimization of the reaction time and catalyst loading can avoid/minimize over-reduction and lead to high yields of silyl acetals, which can be hydrolyzed under mildly acidic condition to give the corresponding aldehydes (Scheme 1). A biphasic extraction method was employed for the separation of aldehydes from siloxane by-products and eliminated the need for column chromatography in most cases.[8]

The results of iridium-catalyzed reductions of a variety of esters using diethylsilane are shown in Table 2. The reductions proceed with low catalyst loading (0.1–0.5 mol %) under mild reaction condition (RT–50 °C) and are compatible with various functionalities including aryl halides, alkyl halides, ethers, alkenes, alkynes, tertiary amines, nitriles, hydroxy, and sulfonyl groups. In this study, ethyl esters were chosen as the primary substrates because of their commercial availability and the easy removal of the ethanol by-product, although esters with other R^2 groups such as methyl or benzyl are also suitable substrates. The iridium catalyst is not compatible with nitro groups: reaction with ethyl 4-nitrobenzoate led to insoluble and unidentified products. Finally, this catalytic system does competitively hydrosilylate carbonyl groups in amides, aldehydes, and ketones.

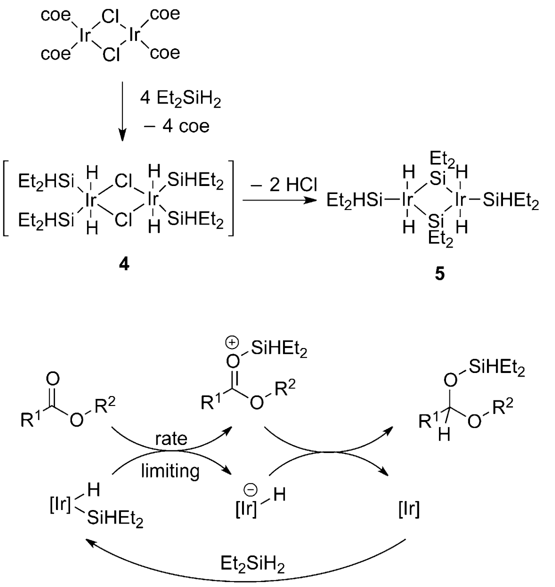
We propose that the catalytically active species is a binuclear silylene-bridged iridium dimer formed by sequential displacement of the cyclooctene and chloride ligands on $[\{Ir(coe)_2Cl\}_2]$ (Scheme 2). An analogous complex prepared

Table 2: Reduction of esters to aldehydes through hydrosilylation.[a]



Entry	Ester		T [°C]	t [h]	Conversion [%][b]	Yield [%][c]
1		**1a**	23	1	>99	95 (76)
2[d]		**1a**	23	1	>99	95
3		**1b**	23	2	99	99
4		**1c**	23	1	>99	99
5		**1d**	50	1	>99	99 (78)
6		**1e**	50	1	>99	94 (73)
7		**1f**	50	1	>99	97 (71)
8		**1g**	23	3	>99	99 (90[e])
9		**1h**	23	7	>99	99 (67)
10		**1i**	23	1	97	96 (60)
11		**1j**	23	1	>99	98 (47[g])
12[f]		**1k**	23	1	>99	98 (74)
13		**1l**	23	4	99	99 (68[g])
14[f]		**1m**	50	9	90	90 (70)
15		**1n**	23	3	>99	99 (82)
16		**1o**	50	7	97	96 (77)
17		**1p**	50	4	>99	99 (75[e])
18[f]		**1q**	50	4	90	90 (74[e])
19		**1r**	23	2	>99	99 (79[g])
20[f,h]		**1s**	50	2	>99	–[i] (37[g])

[a] Reaction conditions: ester (1.0 mmol) with $[\{Ir(coe)_2Cl\}_2]$ (0.9 mg, 1 μmol) and Et_2SiH_2 (130 mg, 1.5 mmol) in CH_2Cl_2 (0.5 mL). [b] Determined by ^1H NMR spectroscopy. [c] Yields of **2** determined by ^1H NMR spectroscopy. The numbers in parenthesis are the yields of isolated **3**. [d] Reaction run in the presence of benzyl chloride or benzyl bromide (1.0 mmol), which remained unreacted throughout the reaction. [e] Isolated as the 2,4-dinitrophenylhydrazone adduct. See Ref. [9]. [f] 4.5 mg (0.5 mol %) $[\{Ir(coe)_2Cl\}_2]$ was used. [g] Purified by column chromatography. [h] 2.5 equiv Et_2SiH_2 was used. [i] Unable to determine the NMR yield.



Scheme 2. Proposed catalytically active species and catalytic cycle.

from tBu$_2$SiH$_2$ was previously characterized by X-ray crystallography to confirm the bridging silylene structure.[6] Since tertiary silanes cannot easily form the dimer species **5** (such a reaction would require Si–C bond cleavage),[10] it is not surprising that only secondary silanes showed significant activities in this catalytic system (Table 1). In the catalytic cycle, transfer of "Et$_2$HSi$^+$" to the carbonyl oxygen appears to be rate-limiting as seen by reduced reaction rates in electron-deficient substrates (Table 2, entry 1 vs entry 18). Substrates with strongly coordinating groups retard the rate of reaction and require higher temperatures or higher catalyst loadings (see entry 14).

In summary, we have demonstrated that aldehydes can be prepared from esters via hydrosilylation using Et$_2$SiH$_2$/[{Ir(coe)$_2$Cl}$_2$] followed by hydrolysis of silyl acetals. Featuring low catalyst loadings of a commercially available iridium complex, mild reaction conditions, high yields, easy product isolation, and good functional group compatibility, this method is an attractive new procedure for preparing aldehydes from esters.

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Keywords: aldehyde synthesis · ester reduction · homogeneous catalysis · hydrosilylation · iridium catalysis

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[7] For methyl and benzyl esters screened, over-reduction was not observed even at elevated temperature, whereas ethyl esters undergo up to ca. 5% further reduction (C–O bond cleavage) under this condition. It is not clear how the reactivity of the silyl acetals toward further reduction depends on the R^2 group.

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[9] The aldehyde products **3g** and **3q** are volatile, and **3p** decomposed during normal workup (both by extraction-based method and column chromatography). Thus, the yields were better gauged by converting these aldehydes to the corresponding 2,4-dinitrophenylhydrazone adduct in situ and isolating the hydrazones. See: M. Behforouz, J. L. Bolan, M. S. Flynt, *J. Org. Chem.* **1985**, *50*, 1186–1189, and Supporting Information.

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