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Reductive etherification of aldehydes photocatalyzed by dicarbonyl pentamethylcyclopentadienyl iron complexes

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ABSTRACT

The reductive etherification of aldehydes can be performed by the reaction with dialkylmethylsilanes in the presence of new iron(II) piano-stool catalysts of general formula Cp*Fe(CO)₂Ar (Cp* = η^5 -C₅Me₅; Ar = Ph, 4-C₆H₄OCH₃, 4-C₆H₄CH₃, Fc). This transformation is promoted by UV light and affords a simple route for the preparation of unsymmetrical alkyl ethers.

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In recent years, there has been continuing interest in the catalyzed reductive etherification of carbonyl compounds because the ether linkage is one of the most important functional groups in organic chemistry.^{1–13} This valuable transformation involves the use of organosilanes with aldehydes or ketones in the presence of a Lewis acid catalyst, carried out under very mild reaction conditions to limit the formation of side products (in contrast to more classical methods such as the Williamson synthesis), and thus give symmetrical or unsymmetrical ethers in high yields. Typically, carbonyl compounds are converted into mixed ethers with trimethylsilyl ethers (or the corresponding unprotected alcohol) as the alkoxy source and triethylsilane as the reductant (Scheme 1).

Various Lewis acids, ranging from metal salts such as $InCl_{3,}^{3}$ FeCl₃,⁴ BiCl₃,⁸ or Cu(OTf)₂⁷ to metal-free species such as TMSI,¹¹ TMSOTf,¹⁰ or triflic acid,¹ have been examined and proved to be efficient catalysts in this reductive coupling. However, we believe that despite the diversity and the usefulness of the previous catalytic systems, development of practical and original procedures for this transformation remains desirable.

Half-metallocene iron(II) carbonyl complexes incorporating $[CpFe(CO)_n]$ or $[Cp^*Fe(CO)_n]$ fragments (n = 1 or 2; Cp: cyclopentadienyl = η^5 -C₅H₅; Cp*: pentamethylcyclopentadienyl = η^5 -C₅Me₅) have been used as Lewis acid catalysts since the early 1980s for various organic transformations such as C–C bond formation, reduction of carbonyl compounds, living radical polymerization,



Scheme 1. Synthesis of unsymmetrical ethers by reductive etherification of carbonyl compounds.

or Diels–Alder and other cycloaddition reactions.¹⁴ Interest in these molecules is currently growing due to the abundance, sustainability, and non-toxicity of iron, in conjunction with the versatility and selectivity of iron complexes in catalysis.¹⁵ With the last-mentioned in mind, we have now prepared and fully characterized a series of piano-stool iron(II) σ –aryl complexes of general formula Cp*Fe(CO)₂Ar and found that representatives of a family of such molecules display good catalytic activity for the UV-promoted reductive etherification of aromatic and aliphatic aldehydes.

The iron precatalysts $Cp^*Fe(CO)_2Ar$ (Ar = Ph (2); (4-C₆H₄OCH₃) (3); (4-C₆H₄CH₃) (4); Fc (5)) were synthesized as shown in Scheme 2. When treated with phenyllithium or lithiobenzene derivatives, the readily accessible iodo precursor $Cp^*Fe(CO)_2I$ (1)¹⁶ undergoes a substitution reaction to give the desired complexes 2–4. A similar reaction of 1 with monolithioferrocene, prepared according to the procedure of Mueller–Westerhoff,¹⁷ gives the homodinuclear iron product 5. After purification, these compounds were obtained as air-stable yellow solids in fair to good yields.

While considerable recent efforts have been focused on optimizing the syntheses of a wide range of parent $CpFe(CO)_2Ar$ derivatives,¹⁸ the metathesis of **1** with aryllithium reagents that we



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Scheme 2. Synthesis of precatalysts 2-5.

have employed possibly constitutes the most straightforward route to the molecules depicted here although, to the best of our knowledge, only one representative of this family, that is Cp*Fe(-CO)₂(2,6-C₆H₃F₂), has been previously synthesized following this protocol.¹⁹ The new complexes were readily identified by the usual spectroscopies and satisfactory high-resolution mass spectrometry and elemental analyses were obtained. The crystal structures of **2**–**5** were unequivocally determined by X-ray diffraction analyses, as illustrated for **5** in Figure 1, and can be described as distorted three-legged piano-stool iron complexes with bond lengths and angles within the previously established ranges.¹⁶ They are essentially symmetrical with respect to the plane bisecting the Fe(CO)₂ unit.

We then investigated the catalytic activity of iron carbonyl compounds **2–5** for the reaction of aldehydes with functional silanes under irradiation. First, 4-bromobenzaldehyde as the model substrate was treated with 1.5 equiv of diethoxymethylsilane under UV light, in the presence of complexes **2–5** at a catalytic loading of 2 mol % (Table 1). After 4 h of irradiation, full conversion of the aldehyde was achieved and only 1-bromo-4-(ethoxymethyl)benzene was isolated in high yields following hydrolysis (runs 2–5).

The following comments can be made: (1) No reaction is observed in the absence of catalyst (run 1). (2) Methylene chloride



Figure 1. Molecular diagram of compound **5** at the 40% probability level. All hydrogen atoms have been omitted for clarity. Selected bond distances (Å) and angles (deg): Fe(1)-C(11) 1.752(2), Fe(1)-C(13) 1.760(2), Fe(1)-C(21) 1.985(0), C(11)-O(12) 1.152(2), C(13)-O(14) 1.148(2), $Fe(1)-Cp^*_{centroid} 1.729$, $Fe(2)-Cp_{centroid} 1.653$, C(11)-Fe(1)-C(13) 96.48(9), C(11)-Fe(1)-C(21) 90.57(8), C(13)-Fe(1)-C(21) 90.81(8), O(12)-C(11)-Fe(1) 177.2(5), $O(14)-C(13)-Fe(1)-Cp^*_{centroid} 124.58$, $C(13)-Fe(1)-Cp^*_{centroid} 124.74$.

Table 1



СНО	1) (EtO) ₂ MeSiH, DCM <u>cat. [Fe], hV, 4</u> h	A CONTRACTOR
Br	2) Hydrolysis	Br
Run ^a	Catalyst	Yield ^b (%)
1	None	0
2	2	88
3	3	93
4	4	95
5	5	88

^a All reactions were carried out with 2 mmol of 4-bromobenzaldehyde, 1.5 equiv of silane, and 0.02 equiv of the catalyst.

^b Isolated yields.

is the solvent of choice for this reaction; in comparison, acetonitrile or toluene gives poor conversions even after longer reaction times. (3) Attempts performed under various conditions without UV light were unsuccessful. (4) The diethoxymethylsilane provides the ethoxy group of the isolated ether and presumably acts as the hydride source during the reaction, since the substrate was recovered when diphenylsilane was used in its place.

Next, the scope and limitations of this iron-catalyzed reductive etherification were investigated with **3** as the model catalyst and a variety of aromatic aldehydes under the same reaction conditions (Table 2, runs 1–9). Benzaldehyde (run 1) and its alkylated (run 6) or halogenated (runs 2, 4 and 7) derivatives were well tolerated. When methyl 4-formylbenzoate was used, etherification of the aldehyde was followed by saponification of the ester and the corresponding benzoic acid product was formed (run 8), but a slight modification of the hydrolysis step allowed to maintain the ester group in the final product (run 9). Surprisingly, when substrates with strong electron-releasing or electron-withdrawing functional groups were tested (runs 3 and 5), the catalytic activity of **3** was lost. Efforts to understand and to overcome these substituent effects (which were also observed with **2**, **4**, and **5**) have so far been unsuccessful.

When dimethoxymethylsilane was used in this reaction (runs 10–14), the expected benzyl methyl ether derivatives were isolated in excellent yields. Particularly noteworthy is that the more sterically hindered *o*-tolualdehyde also gave the desired product in almost quantitative yield (run 14). Furthermore, we have found that this reaction is similarly effective for aliphatic aldehydes such as undecyl aldehyde (run 15) or phenylacetaldehyde (run 16), but with these substrates the hydrolysis step must be avoided to prevent any decomposition of the ether formed, and was replaced by a chromatographic purification.

We believe that the mechanism of this photocatalyzed process can be considered to proceed via an hemiacetal-type intermediate.^{12,13} The active Lewis acid catalysts certainly originate from the photochemical decarbonylation of the precatalysts **2–5** to give 16-electron intermediates of general formula [Cp*Fe(CO)Ar], and not from the cleavage of the σ -bonded aryl ligand leading to the cationic [Cp*Fe(CO)₂]⁺ fragment. Indeed, the photolabilization of CO ligands in Cp*Fe(CO)₂X architectures has been established previously,^{19,20} and when the THF adduct [Cp*Fe(CO)₂(THF)][PF₆]²¹ was employed in the reaction, no transformation occurred.

In conclusion, we have found a new photoinduced reaction for the preparation of unsymmetrical ethers from both aromatic and aliphatic aldehydes. For the first time, stable iron(II) carbonyl complexes activated upon UV irradiation were employed in this reductive etherification. The main advantages of this protocol are rapid and clean conversion of the substrates under mild reaction conditions, low catalytic loadings, and the necessity for only one silane reagent.

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Table 2

Screening of the reaction using **3** as the catalyst

	R		$rac{1}{2}$ R OR'	
Run ^a	Substrate	Silane	Product	Yield ^b (%)
1	СНО	(EtO) ₂ MeSiH		70
2	Br		Br	84
3	O ₂ N CHO	n	O ₂ N O	0
4	СІСНО	'n	CI	91
5	MeO	11	MeO	Trace
6	Me	11	Me	73
7	F CHO	"	F	78
8	Me ⁻⁰ CHO	"	HO ₂ C	94
9 ^c	Me ^{-O} CHO O		Me	75
10	Br	(MeO) ₂ MeSiH	Br	98
11	Me	11	Me	99
12	СНО	"		82
13	CI	"	CI	90
14	CHO	'n		99
15 ^d	(~) 9	(EtO) ₂ MeSiH	(~) O ` 9	70
16 ^d	СНО	,,		70

^a All reactions were carried out with 2 mmol of the substrate, 1.5 equiv of silane, and 0.02 equiv of **3**.

^b Isolated yields.

^c To avoid saponification of the product, the hydrolysis step was modified.

^d Purification of the crude product by chromatography instead of hydrolysis.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012. 07.038.

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