

Iron Trichloride Mediated Allylation of Lithium Alkoxides through an Unusual Carbon–Oxygen Bond Cleavage

George W. Kabalka,* Min-Liang Yao, Scott Borella, and Laura K. Goins†

Departments of Chemistry and Radiology, University of Tennessee, Knoxville, Tennessee 37996-1600

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Summary: Iron trichloride was found to cleave carbon–oxygen bonds in a variety of lithium alkoxides at room temperature. Other Lewis acids were also found to cleave the alkoxides. Acid-sensitive groups are tolerated under the reported reaction conditions.

In the last two decades, considerable effort has been devoted to the cleavage of unreactive bonds, such as carbon–hydrogen,¹ carbon–carbon,² carbon–nitrogen,³ and carbon–oxygen bonds.⁴ Direct cleavage of these bonds provides several advantages in organic syntheses, including atom efficiency, low environmental load, and the potential for unusual chemoselectivity. With respect to carbon–oxygen bond cleavage, significant results have been achieved using alcohols⁵ and ethers.⁶ Herein we wish to report an unusual bond cleavage involving the carbon–oxygen bond in lithium alkoxides (ROLi) in the presence of metal halides (MX_n), including iron, tin, silicon, aluminum, and boron chlorides. This carbon–oxygen cleavage occurs smoothly,

Scheme 1. Transition-Metal-Free Coupling of Alkoxides with Organoboron Dihalides

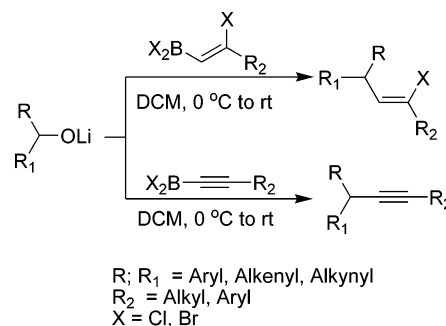
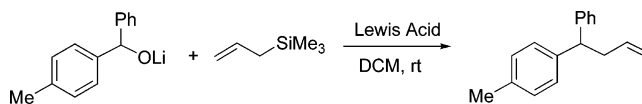


Table 1. Alkoxide Carbon–Oxygen Bond Cleavage Using Lewis Acids^a



entry	Lewis acid	yield (%) ^b	entry	Lewis acid	yield (%) ^b
1	BCl ₃	96 ^c	5	SiCl ₄	27
2	FeCl ₃	95	6	CuCl ₂	0
3	SnCl ₄	77	7	NiCl ₂	0
4	AlCl ₃	77			

^a Reaction carried out at room temperature on a 1.5 mmol scale in dry dichloromethane. ^b Isolated yield based on lithium alkoxide. ^c Reference 12.

even at room temperature, and most likely proceeds through the unstable metal alkoxide complex intermediate [M(OR)_mX_{n-m}].

We have been investigating boron halide chemistry for many years, and a number of novel reactions have been developed.⁷ Recently, we reported the transition-metal-free coupling of alkoxides with alkenylboron dihalides and alkynylboron dihalides (Scheme 1).⁸

Preliminary mechanistic studies revealed that these reactions apparently proceed through cation intermediates.^{8b} In a continuation of these studies, we discovered that this type of carbon–oxygen bond cleavage can be achieved using FeCl₃. To the best of our knowledge, direct carbon–oxygen bond cleavage in an alkoxide by a metal halide is unknown,⁹ although β-hydrogen¹⁰ and β-hydrocarbyl¹¹ eliminations in the transition-metal alkoxide complexes [M(OR)_mX_{n-m}], generated in situ, have been documented.

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* To whom correspondence should be addressed. Phone: (865) 974-3260. Fax: (865) 974-2297. E-mail: kabalka@utk.edu.

† Current address: Department of Chemistry, Emory University, Atlanta, GA.

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Table 2. Iron Trichloride Mediated Allylation of Lithium Alkoxides¹⁸

Alkoxide (1)		Product (2)	Yield (%) ^{a,b}
	1a: Z = <i>p</i> -Me	2a	95
	1b: Z = H	2b	98
	1c: Z = <i>p</i> -Cl	2c	86
	1d: Z = <i>o</i> -Me	2d	93
	1e: Z = <i>p</i> -CN	2e	40
	1f	2f	71
	1g	2g	75
	1h	2h	96
	1i	2i	80
	1j	2j	83
	1k	2k	68
	1l: Z = Cl	2l	74
	1m: Z = H	1m	32
	1n	2n	78

^a Reaction carried out at room temperature on a 1.5 mmol scale in dry dichloromethane.¹⁸ ^b Isolated yield based on the alkoxide.

The reaction of the lithium salt of phenyl-*p*-tolylmethanol with allyltrimethylsilane was chosen as the model reaction to evaluate the breadth of the new cleavage reaction. Several Lewis acids were screened, and the results are illustrated in Table 1.

As demonstrated by the data in Table 1, several Lewis acids successfully cleave the carbon–oxygen bond in the alkoxide. Comparable results were obtained with boron trichloride¹² and

(9) Scattered reports describe the carbon–oxygen bond cleavage in isolated metal alkoxide complexes; see: (a) Kawaguchi, H.; Matsuo, T. *J. Am. Chem. Soc.* **2003**, *125*, 14254. (b) Fandos, R.; Hernández, C.; Otero, A.; Rodríguez, A.; Ruiz, M. J.; Terreros, P. *Dalton Trans.* **2002**, 11. (c) Baumann, R.; Stumpf, R.; Davis, W. M.; Liang, L.-C.; Schrock, R. R. *J. Am. Chem. Soc.* **1999**, *121*, 7822.

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iron trichloride (96% vs 95%). Interestingly, iron trichloride has been reported to be an ineffective catalyst for the allylation of benzylic alcohols using allyltrimethylsilane,^{13,14} and reactions

(11) For observation of β -hydrocarbyl eliminations in the isolated metal alkoxide complexes [M(OR)_mX_{n-m}], see: (a) Hartwig, J. F.; Bergman, R. G.; Andersen, R. A. *Organometallics* **1991**, *10*, 3344. (b) Zhao, P.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 3124. For examples of β -hydrocarbyl eliminations in catalytic processes, see: (c) Kondo, T.; Kodoi, K.; Nishinaga, E.; Okada, T.; Morisaki, Y.; Wantanabe, Y.; Mitsudo, T. *J. Am. Chem. Soc.* **1998**, *120*, 5587. (d) Funayama, A.; Satoh, T.; Miura, M. *J. Am. Chem. Soc.* **2005**, *127*, 15354.

(12) In a similar study, the direct allylation of propargylic alkoxides was found to proceed through cationic intermediates using boron trichloride. See: Kabalka, G. W.; Yao, M.-L.; Borella, S. *J. Am. Chem. Soc.* **2006**, *128*, 11320.

(13) De, S. K.; Gibbs, R. A. *Tetrahedron Lett.* **2005**, *46*, 8345.

(14) Zhan and co-workers have reported an iron trichloride catalyzed allylation of propargylic alcohols with allyltrimethylsilane. See: Zhan, Z.-p.; Yu, J.-I.; Liu, H.-j.; Cui, Y.-y.; Yang, R.-f.; Yang, W.-z.; Li, J.-p. *J. Org. Chem.* **2006**, *71*, 8298.

using a stoichiometric amount of iron trichloride generally lead to an inseparable mixture of the allylation product along with the HCl addition product.¹⁵ The separation problems related to the HCl addition product, together with other issues¹⁶ related to the high acidity of the reaction,¹⁷ can be overcome by using alkoxides as the reactants. Iron trichloride was chosen to evaluate the scope of the cleavage reaction due to its low cost (Table 2).

All reactions utilizing secondary allylic, propargylic, and benzylic alkoxides produced the desired products in moderate to high yields. Attempts to cleave the carbon–oxygen bond in primary benzylic alkoxides and secondary aliphatic alkoxides were unsuccessful. The carbon–oxygen bond cleavage in tertiary alkoxides is remarkable because complexes bearing tertiary alkoxide ligands have been reported to undergo β -hydrocarbyl eliminations to form an organometal intermediate along with a ketone.^{11d,19} The regioselective allylation of propargylic alkoxides is significant, since this transformation traditionally relies on the Nicholas reaction²⁰ (a multistep reaction involving transition-metal-stabilized propargylic cations).

Though a detailed mechanistic study has not been undertaken, potential driving forces for the reaction include steric interactions between the organic substituents and the chlorine, the crystal lattice energy of LiCl, and the strength of the Fe–O bond. A similar cleavage has been proposed recently in the $\text{TiCl}_4/\text{R}_3\text{N}$ -mediated conversion of propargyl alcohols to chloroallenes.²¹ The formation of an oxonium ion intermediate via $[\text{RR}_1\text{CHO}(\text{FeCl}_3)\text{FeCl}_2]$ would be in line with Lewis acid catalyzed allylation reactions of acetates^{14,22} and silyl ethers.²³ In addition, 1-phenylcyclopentene (**5**) was isolated during the allylation of

(15) HCl is the unavoidable side product from the direct allylation of alcohol with allyltrimethylsilane. In most cases it subsequently adds to the carbon–carbon double bond in the allylation product.

(16) Rubin, M.; Gevorgyan, V. *Org. Lett.* **2001**, *3*, 2705.

(17) To overcome problems in the direct allylation of alcohols using strong acids, a combination of weak Lewis acids to enhance the Lewis acidity of the reaction system was reported recently. See: (a) Saito, T.; Yasuda, M.; Baba, A. *Synlett* **2005**, 1737. (b) Saito, T.; Nishimoto, Y.; Yasuda, M.; Baba, A. *J. Org. Chem.* **2006**, *71*, 8516.

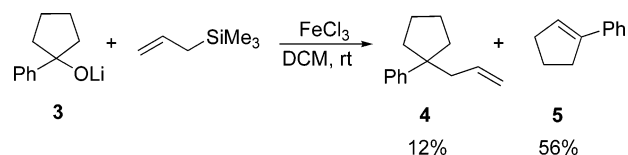
(18) Typical experimental procedure: a solution of alcohol (1.5 mmol) in dry dichloromethane (10 mL) was treated with *n*-butyllithium (1.0 mL of a 1.6 M solution in hexanes) at 0 °C and the solution warmed to room temperature. After the mixture was stirred at room temperature for 30 min, allyltrimethylsilane (1.8 mmol) and iron trichloride (1.6 mmol) were added. The mixture was stirred for 6 h. Water (20 mL) was added to quench the reaction, the mixture was extracted with ethyl acetate, and the extracts were then dried over anhydrous MgSO_4 . The solvent was removed in vacuo and the product purified by silica gel column chromatography using hexane as an eluent.

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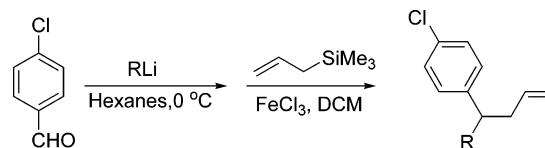
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Scheme 2. Evidence Supporting a Cationic Mechanism



Scheme 3. Tandem Reaction



R = Ph: **2c**, 73%; R = Ph-C \equiv C: **6**, 64%

alkoxide **3** (Scheme 2). Although **5** could, in theory, be formed via an E₂ elimination from the initial (benzyloxy)iron chloride, the absence of a base would appear to make this unlikely.

The iron trichloride mediated coupling reaction of alkoxides with allyltrimethylsilane also makes tandem reactions feasible, since most secondary and tertiary alcohols can be prepared in situ from the reaction of aldehydes and alkyllithium reagents (Scheme 3).

The cleavage of a carbon–oxygen bond in a metal alkoxide by a Lewis acid under such mild reaction conditions is unique. From the viewpoint of organic synthesis, this iron trichloride mediated coupling reaction can be viewed as a substitution of the OFeCl_2 group. On the basis of the facile reaction of $[\text{RR}_1\text{CHOFeCl}_2]$ with allylsilane, OFeCl_2 appears to be more effective than traditional leaving groups, such as OAc, OTf, and OTs. Further investigations using this methodology are under way.

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Supporting Information Available: Text and figures giving details of the syntheses and characterization data for the new compounds prepared in this paper. This information is available free of charge via the Internet at <http://pubs.acs.org>.

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