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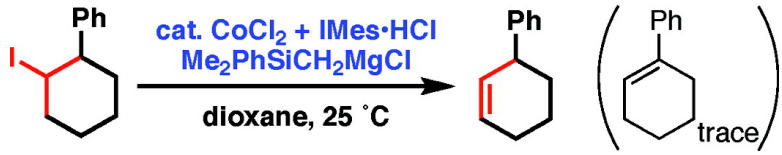

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Cobalt-Catalyzed Regioselective Dehydrohalogenation of Alkyl Halides with Dimethylphenylsilylmethylmagnesium Chloride

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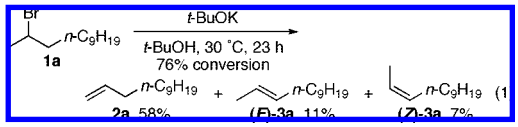
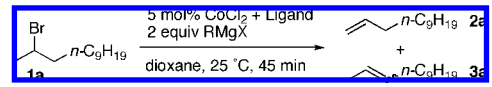
A base-mediated dehydrohalogenation reaction is among the most basic organic reactions. However, regio- and stereochemical control of the reaction are not easy, as clearly demonstrated in the historical study by Bartsch.[1] For instance, treatment of 2-bromododecane (**1a**) with potassium *tert*-butoxide in *tert*-butyl alcohol for 1 d afforded a mixture of 1-dodecene (**2a**), (*E*)-2-dodecene [(*E*)-**3a**], and (*Z*)-2-dodecene [(*Z*)-**3a**] (eq 1). There are some studies aiming at selective dehydrohalogenation reactions,[1,2] which failed to attain high selectivity or lacked generality.[3] Development of regio- and stereoselective dehydrohalogenation that is applicable to modern organic synthesis has been awaited.



Here we report the cobalt-catalyzed highly regioselective dehydrohalogenation reaction of alkyl halides with a Grignard reagent. Treatment of **1a** with $Me_2PhSiCH_2MgCl$ in the presence of catalytic amounts of cobalt(II) chloride and a precursor of an *N*-heterocyclic carbene IMes•HCl[4] afforded **2a** selectively (Table 1, entry 1). The use of a bulkier carbene ligand IPr•HCl[4] as well as Mes•HASPO[5] ligand resulted in lower reaction efficiency and lower **2a**/**3a** selectivity (entries 2 and 3). Phosphine ligands were inferior to the carbene ligands with respect to both reactivity and selectivity (entries 4−6). Bidentate ligands completely suppressed the catalytic activity of cobalt (entries 7 and 8). The choice of the Grignard reagent is important. Only silyl-substituted methylmagnesium reagents promoted the elimination reaction. Me_3SiCH_2MgCl served well, albeit with lower **2a**/**3a** selectivity (entry 9). The reactions with methyl and allyl Grignard reagents led to poor conversions (entries 10 and 11). The uses of BuMgBr and PhMgBr afforded dodecane mainly (entries 12 and 13).

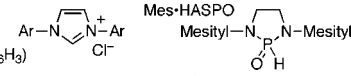
A variety of 2-bromoalkanes were transformed into terminal alkenes with high regioselectivity (Table 2). The cobalt-catalyzed dehydrobromination was applicable to substrates containing *tert*-butyldimethylsiloxy, *p*-toluenesulfonylamino, chlorophenoxy groups, leaving these functional groups untouched (entries 2−4). The low nucleophilicity of the silyl-substituted Grignard reagent allowed for the reactions of aromatic esters (entries 5−7). It is worth noting that all the reactions, except for the reaction of **1c**, provided less than 2% yields of the corresponding internal alkenes. Whereas the reaction of **1i**, having a branched pentyl group at the 4 position of the 2-bromoalkane skeleton, proceeded smoothly (entry 8), the reaction of **1j**, having a methyl group at the 3 position, required a higher temperature to complete the reaction (eq 2). The difference of the reactivities between **1i** and **1j** shows that the elimination reaction is sensitive to the steric environment around the brominated carbon.

Table 1. Cobalt-Catalyzed Dehydrobromination Reactions of 2-Bromododecane



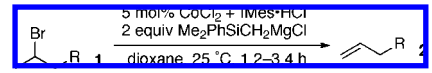
entry	ligand	RMgX	**1a** / %	**2a** / %	**3a** / %
1	IMes•HCl[a]	$Me_2PhSiCH_2MgCl$	0	84	6
2	IPr•HCl[a]	$Me_2PhSiCH_2MgCl$	54	36	4
3	Mes•HASPO[a]	$Me_2PhSiCH_2MgCl$	67	25	8
4	Ph_3P	$Me_2PhSiCH_2MgCl$	89	7	2
5	$(t\text{-Bu})_3P$	$Me_2PhSiCH_2MgCl$	74	17	8
6	$(c\text{-}C_6H_{11})_3P$	$Me_2PhSiCH_2MgCl$	78	20	2
7	DPPE[b]	$Me_2PhSiCH_2MgCl$	98	1	0
8	TMEDA[c]	$Me_2PhSiCH_2MgCl$	100	0	0
9	IMes•HCl	Me_3SiCH_2MgCl	0	74	13
10	IMes•HCl	MeMgI	91	1	1
11	IMes•HCl	$CH_2{=}CHCH_2MgCl$	86	3	3
12[d]	IMes•HCl	BuMgBr	0	4	30
13[e]	IMes•HCl	PhMgBr	25	8	9

[a] IMes•HCl (Ar = Mesityl), IPr•HCl (Ar = 2,6-(*i*-Pr)$_2$C$_6$H$_3$)



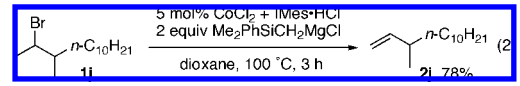
[b] $Ph_2PCH_2CH_2PPh_2$. [c] $Me_2NCH_2CH_2NMe_2$. [d] Dodecane (65%) was obtained. [e] Dodecane (53%) was obtained.

Table 2. Scope of 2-Bromoalkane Derivatives



entry	R	**1**	time /h	**2** /%
1	CH_2-1-naphthyl	**1b**	2	**2b**, 89
2	$(CH_2)_8OSi(t\text{-Bu})Me_2$	**1c**	1.5	**2c**, 86[a]
3	$CH_2CH_2N(CH_2Ph)Ts$	**1d**	2	**2d**, 79
4	$CH_2CH_2OC_6H_4$-*p*-Cl	**1e**	1.2	**2e**, 99
5	$CH_2OC(=O)Ph$	**1f**	3.4	**2f**, 81
6	$CH_2OC(=O)C_6H_4$-*p*-CF_3	**1g**	1.8	**2g**, 70
7	$CH_2OC(=O)$(2-thienyl)	**1h**	3	**2h**, 80
8	$CH(n\text{-}C_5H_{11})_2$	**1i**	1.2	**2i**, 80

[a] (*E*)-$CH_3CH{=}CH(CH_2)_8OSi(t\text{-Bu})Me_2$ [(*E*)-**3c**] was obtained in 4% yield.



The reaction of 2-iododododecane proceeded to completion within 15 min to yield **2a** with excellent selectivity (Table 3, entry 1). On the other hand, the corresponding mesylate and tosylate resisted the elimination reaction (entries 3 and 4). The reaction of 2-chlorododecane was slow (entry 2). Primary alkyl iodide and bromide also underwent the elimination reaction (entries 5 and 6). The reaction of 2-bromo-2-methyltridecane at 50 °C for 1 h afforded a

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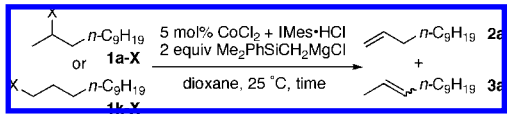
Table 3. Reactions of Other Alkyl Halides and Pseudohalides



entry	1	time /h	1 /%	2a /%	3a /%
1	**1a−I**	0.25	0	87	3
2	**1a−Cl**	3.7	83	13	1
3	**1a−OMs**	2	82	0	0
4	**1a−OTs**	4	97	0	0
5	**1k−I**	0.5	0	96	2
6	**1k−Br**	1.5	0	79	8

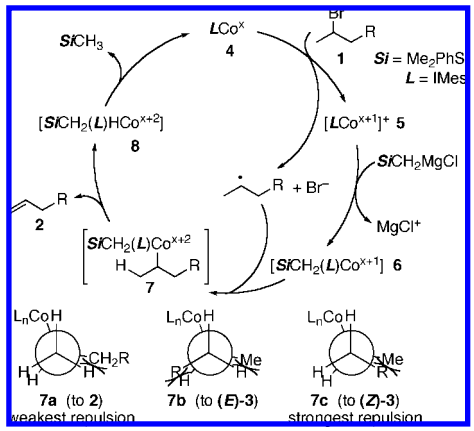
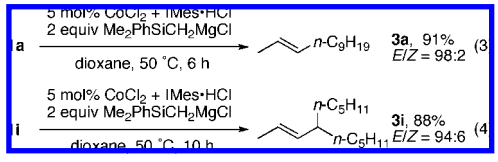


Figure 1. Plausible reaction mechanism and conformational analysis of **7** that undergoes β-elimination.

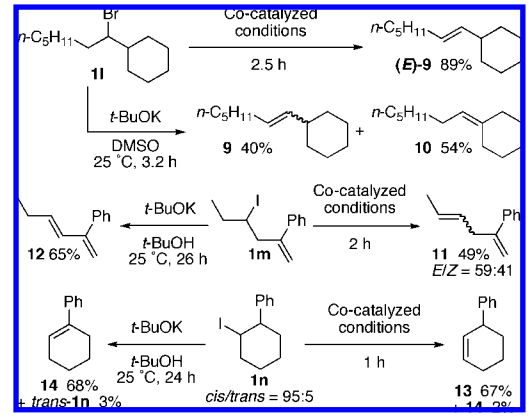
mixture of 2-methyl-1-tridecene (35% yield) and 2-methyl-2-tridecene (51% yield).

Based on our studies on cobalt-catalyzed reactions[6] as well as the reactivity trend observed in Table 3, we are tempted to assume the reaction mechanism as follows (Figure 1). Single electron transfer would take place from electron-rich cobalt complex **4** to an alkyl halide to generate the corresponding alkyl radical.[7] The radical would be then captured by cobalt complex **6** to afford alkylcobalt intermediate **7**. Intermediate **7** would then undergo β-hydride elimination to afford 1-alkene. Degrees of steric repulsion in the transition states of the β-hydride elimination account for the regioselective formation of 1-alkenes. The β-hydride elimination should proceed via a *syn* periplanar conformation **7a**, **7b**, or **7c**.[8] Conformation **7a** is most preferable, minimizing the total steric repulsion.



When the elimination reactions were performed at 50 °C, the corresponding (*E*)-2-alkenes were obtained selectively (eqs 3 and 4). Notably, further isomerization into 3-alkenes is negligible, probably because of the sufficient bulkiness of the cobalt catalyst. The reactions initially afforded 1-alkenes **2** within 15 min, and prolonged heating induced gradual isomerization to (*E*)-alkenes **3**.

Scheme 1. Regioselective Dehydrohalogenation[a]



[a] Co-catalyzed conditions: 5 mol% $CoCl_2$, 5 mol% IMes·HCl, 2 equiv of $Me_2PhSiCH_2MgCl$, dioxane, 25 °C

The interesting reaction mechanism of the cobalt-catalyzed dehydrohalogenation offered unique transformations that are otherwise difficult to attain (Scheme 1). High regioselectivity was observed in the dehydrobromination reaction of **1l**, whereas the reaction of **1l** with *t*-BuOK showed no regioselectivity. The cobalt-catalyzed dehydrohalogenation of homoallyl iodide **1m** selectively yielded unconjugated diene **11**. In contrast, treatment of **1m** with *t*-BuOK provided conjugated diene **12** exclusively. The selective formation of unconjugated alkene **13** in the reaction of **1n** also highlights the synthetic utility of the cobalt catalysis. Notably, most of *trans*-**1n** remained untouched in the *t*-BuOK-mediated dehydroiodination, due to the difficulty in forming the *anti* periplanar transition state for the E2 elimination.

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Supporting Information Available: Experimental details, additional experimental data, and characterization data of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) The single electron transfer mechanism is justified by an additional experiment. For details, see the Supporting Information.
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