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LETTERS

Lanthanum metal-assisted deoxygenative coupling of alcohols

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Abstract—It was found that the deoxygenative coupling of alcohols efficiently proceeded by treatment with lanthanum metal and chlorotrimethylsilane in the presence of a catalytic amount of iodine. This coupling reaction was accelerated by the addition of a catalytic amount of copper(I) iodide. © 2002 Elsevier Science Ltd. All rights reserved.

The reductive coupling of alkyl halides to the corresponding alkanes is a useful method for constructing carbon–carbon bonds, and it can be accomplished with various reagents.[1] Alcohols are easily purchased from commercial sources and alkyl halides are generally synthesized from the corresponding alcohols.[2] Therefore, development of a deoxygenative coupling method of alcohols in organic synthesis is of interest, however, there are only a few reports on the transformation. To the best of our knowledge, low-valent titanium[3] and niobium[4] compounds prepared by the reduction of metal halides are limited reagents for the deoxygenative coupling of alcohols. We now found that lanthanum metal assisted the deoxygenative coupling of alcohols in the presence of chlorotrimethylsilane and a catalytic amount of iodine to give the corresponding coupling products in moderate to good yields. In addition, it was clearly shown that the reaction was accelerated by the addition of a catalytic amount of copper(I) iodide (Scheme 1).

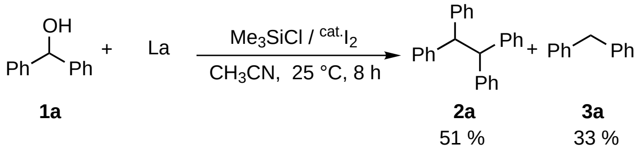
When benzhydrol (**1a**) was treated with lanthanum metal (1 equiv.), chlorotrimethylsilane (2 equiv.) and a catalytic amount of iodine (0.2 equiv.) in acetonitrile solvent at 25°C for 8 h, the deoxygenative coupling of **1a** proceeded smoothly to give 1,1,2,2-tetraphenylethane (**2a**) in 51% yield along with the formation of diphenylmethane (33%) (**3a**) (Scheme 2). The use of THF, which is widely utilized in organic reaction with lanthanoid metal compounds, as the solvent led to a decrease in the yield of **2a** (6%). It is interesting to note that an addition of a catalytic amount of copper(I) iodide (0.2 equiv.) markedly promoted the deoxygenative coupling of **1a** to give **2a** in 87% yield (Scheme 3).[5]

Various alcohols were treated with lanthanum metal and chlorotrimethylsilane in the presence of a catalytic amount of iodine and copper(I) iodide in acetonitrile solvent, and the results are shown in Table 1.[6] 2,3-Diphenylbutane (**2c**) was obtained in 72% yield by the reaction of α-phenethylalcohol (**1c**) with lanthanum metal. For the tertiary alcohol (**1b**), the yield of the deoxygenative coupling product (**2b**) was slightly decreased due to the increase in the yield of 2-phenylpropene (**4b**) as a by-product. When benzyl alcohol (**1d**) was treated with lanthanum metal under the same reaction conditions as **1a**, the yield of 1,2-diphenylethane (**2d**) was 42% and the starting material was 30% recovered. This transformation can be applied to allylic alcohols. For example, similar treatment of 2-cyclohexene-1-ol (**1j**) with lanthanum metal produced 3,3′-bicyclohexenyl (**2j**) in 75% yield. Similarly, cinnamyl alcohol (**1i**) was deoxygenatively coupled to give the corresponding coupling products with a mixture of isomers.

It is already known that the reaction of alcohols with iodotrimethylsilane forms the corresponding iodides in

$$\underset{\mathbf{1}}{\text{R–OH}} + \text{La} \xrightarrow[\text{CH}_3\text{CN}]{\text{Me}_3\text{SiCl / }^{\text{cat.}}\text{I}_2\text{ / }^{\text{cat.}}\text{CuI}} \underset{\mathbf{2}}{\text{R–R}}$$

Scheme 1.



Scheme 2.

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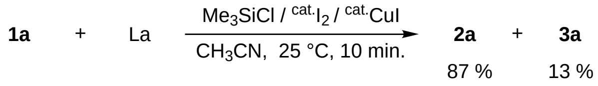
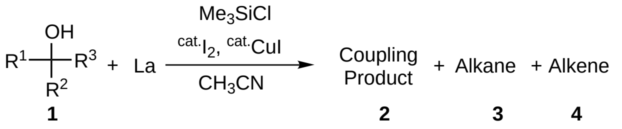


Scheme 3.

Table 1. Deoxygenative coupling of various alcohols with La metal[a]



1	R^1	R^2	R^3	Yield (%)[b]		
				2	3	4
1b	C_6H_5	CH_3	CH_3	**2b** 54	**3b** 13	**4b** 29
1c	C_6H_5	CH_3	H	**2c** 72[c]	**3c** 11	**4c** 6
1d	C_6H_5	H	H	**2d** 42	**3d** 15	–
1e	p-CH_3O-C_6H_4	H	H	**2e** 67	**3e** 5	–
1f	p-CH_3-C_6H_4	H	H	**2f** 59	**3f** 10	–
1g	p-Cl-C_6H_4	H	H	**2g** 34	**3g** 18	–
1h	p-CN-C_6H_4	H	H	**2h** 0	**3h** 0	–
1i	$C_6H_5CH{=}CH$	H	H	**2i** (71)[d]	N.q.[e]	N.q.[e]
1j	$-CH{=}CH-(CH_2)_3-$		H	**2j** 75[c]	N.q.[e]	N.q.[e]

[a] Reaction conditions: alcohol (1.0 mmol), lanthanum metal (1.0 mmol), Me_3SiCl (2.0 mmol), I_2 (0.2 mmol), CuI (0.2 mmol) and CH_3CN (3.0 mL) at 82°C for 1 h.

[b] GC yield. The number in parentheses indicates isolated yield.

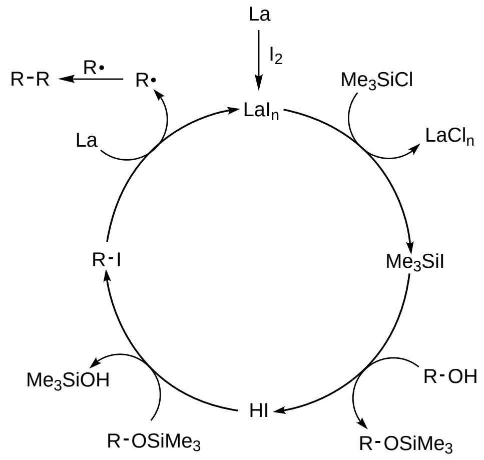
[c] *Dl*:*meso* = 1:1.

[d] 1,6-Diphenyl-1,5-hexadiene:1,4-diphenyl-1,5-hexadiene:3,4-diphenyl-1,5-hexadiene = 32:49:19.

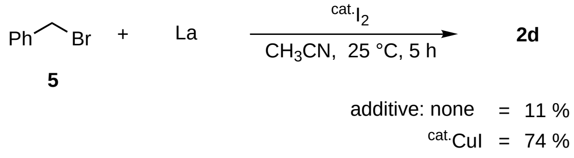
[e] Not quantified.

good yields.[7,8] We have recently found that alkyl iodides were reductively coupled by lanthanum metal to give the corresponding coupling products.[9] Based on these results, the following reaction pathway involving the formation of alkyl iodides was proposed: (i) the generation of lanthanum iodide species (LnI_n) by the reaction of lanthanum metal with iodine, (ii) halogen exchange reaction of Me_3SiCl with LnI_n to form Me_3SiI,[10,11] and (iii) the reaction of alcohols with Me_3SiI to form alkyl iodide. In the absence of copper(I) iodide, alkyl iodides were reductively coupled by lanthanum metal and/or low-valent lanthanum species to give the corresponding coupling products, and the lanthanum iodide species (LnI_n) was regenerated (Scheme 4). The deoxygenative coupling of alcohols was markedly promoted by the addition of a catalytic amount of copper(I) iodide. To obtain information on the role of copper(I) iodide, the reaction of benzyl bromide (**5**) with lanthanum metal was performed in the presence and absence of copper(I) iodide. The treatment of **5** with lanthanum metal in the presence of a catalytic amount of iodine and copper(I) iodide (0.2 equiv.) in acetonitrile at 25°C for 5 h gave 1,2-diphenylethane (**2d**) in 74% yield; however, in the absence of copper(I) iodide, the reaction was extremely slow (11%) (Scheme 5). Ebert et al. have already reported that the reaction of benzyl and allyl halides with activated copper was completed in only 10 min, giving the reductive coupling products in almost quantitative yields.[12] These results suggested that activated copper, which was generated by the reduction of copper(I) iodide with lanthanum metal and/or low-valent lanthanum species, accelerated the coupling reaction of alkyl iodides (Scheme 6).[13]

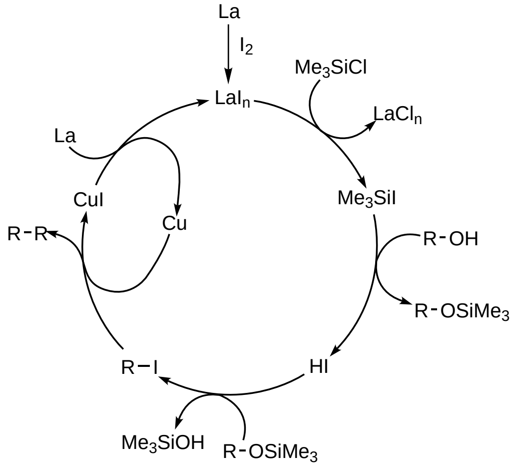
Ether and ester are also readily deoxygenatively coupled by the use of La/Me_3SiCl/$^{cat.}I_2$/$^{cat.}$CuI system. 3-Heptyloxy-cyclohexene (**6**) or 3-acetoxycyclohexene (**7**) was treated with lanthanum metal and chlorotrimethylsilane in the presence of a catalytic amount of iodine, copper(I) iodide and H_2O (0.2 equiv.) to form 3,3′-bicyclohexenyl (**2j**) in 81 and 57% yields, respectively (Scheme 7).[14]



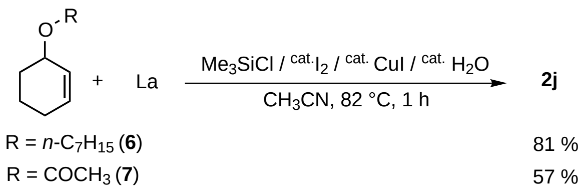
Scheme 4. A possible reaction path.



Scheme 5.



Scheme 6. A possible path in the presence of a catalytic amount of CuI.



Scheme 7.

In summary, it was found that the deoxygenative coupling of alcohols, ethers and esters efficiently proceeded by the treatment of lanthanum metal and chlorotrimethylsilane in the presence of a catalytic amount of iodine and copper(I) iodide.

Acknowledgements

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6. **General procedure**: Lanthanum powder (139 mg, 1 mmol), iodine (51 mg, 0.2 mmol) and copper(I) iodide (36 mg, 0.2 mmol) were placed in a three-necked flask. Alcohol (1 mmol) in CH_3CN (3 mL) and chlorotrimethylsilane (217 mg, 2.0 mmol) were added, and the mixture was stirred at 82°C for 1 h under a nitrogen atmosphere. The color of the solution gradually changed to gray. After the reaction, aq. HCl (1 M, 5 mL) was added to the reaction mixture and extracted with benzene (20 mL×5). The organic layer was dried over $MgSO_4$. The resulting mixture was filtered and the filtrate was concentrated. Purification of the residue by HPLC afforded the corresponding deoxygenative dimerization, deoxygenation and dehydration products. Products were characterized by comparison of their spectral data (^1H and ^{13}C NMR and IR) with those of authentic samples.
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10. Krüerke has reported that Me_3SiI was generated by the reaction of Me_3SiCl with magnesium(II) iodide in CH_3CN. See: Krüerke, U. *Chem. Ber.* **1962**, *95*, 174.
11. In the absence of iodine, deoxygenative coupling of **1a** did not occur; however, the use of iodotorimethylsilane instead of chlorotrimethylsilane gave the deoxygenative coupling product of **1a** in 41% yield. These results might strongly suggest the generation of iodotrimethylsilane by the reaction of chlorotrimethylsilane with lanthanum metal in the presence of a catalytic amount of iodine.
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13. Active zero-valent copper has been commonly prepared by the reduction of a copper(I) halide phosphine complex by lithium naphthalenide. See: Reike, R. D.; Sell, M. S.; Klein, W. R.; Chen, T.; Brown, J. D.; Hanson, M. V. *Active Metals*; Fürstner, A., Ed.; VCH Publishers: New York, 1995, pp. 33–48 and references cited therein.
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