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o-Trimethylsilylphenyllithium as a Synthetic Equivalent of *o*-Halophenyllithium

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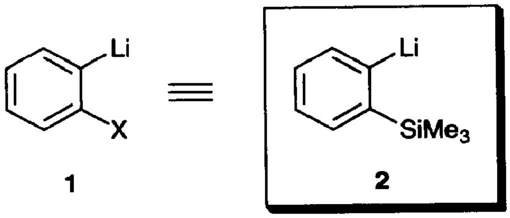
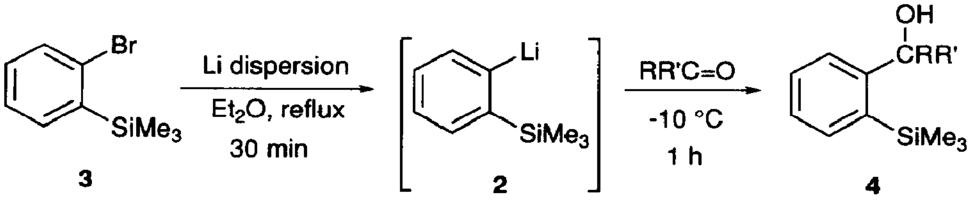
Abstract: The reaction of *o*-trimethylsilylphenyllithium with carbonyl compounds and subsequent halogenodesilylation with ICl afforded *o*-iodophenylcarbinols in good yields, showing the usefulness of *o*-trimethylsilylphenyllithium as a synthetic equivalent of *o*-iodophenyl anion. The reaction *via* a protected *o*-trimethylsilylphenylcarbinol is also shown.

o-Halophenyllithium **1**, in particular *o*-iodophenyllithium, is a useful synthon for constructing a benzo component of variously benzo-fused molecules *via* stepwise coupling reactions with complementary moiety of the targeted molecules. While the generation of *o*-chlorophenyllithium or *o*-chlorophenylmagnesium bromide has been reported in the literature,[1,2] *o*-bromo- or *o*-iodophenyllithium is known to be difficult to be used in organic synthesis because of its propensity to release *o*-halogen forming benzyne even at a low temperature.[3-5]

We took notice the fact that trimethylsilylbenzenes are easily converted to halogenobenzenes by halogenodesilylation reaction,[6,7] and expected that *o*-trimethylsilylphenyllithium (**2**) might serve as a synthetic equivalent of **1**. Here, we report the realization of the expectation in the preparation of various *o*-iodophenylcarbinols as a typical example.



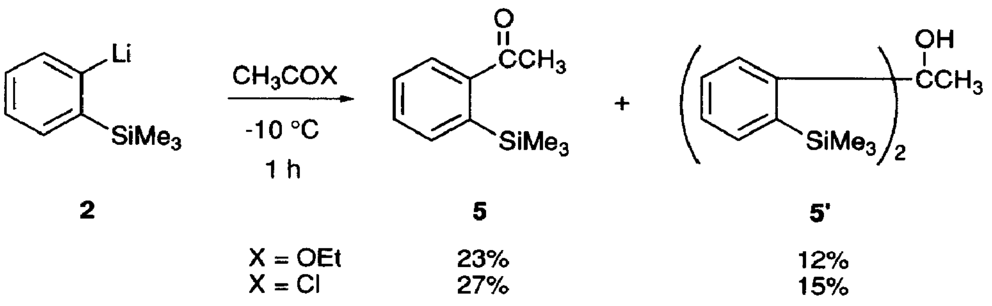
o-Trimethylsilylphenyllithium (**2**) was prepared *in situ* by lithiation of *o*-bromo(trimethylsilyl)benzene (**3**)[6] with lithium dispersion in ether (reflux, 30 min). The reaction of **2** with D_2O afforded *o*-deuterio(trimethylsilyl)benzene in 80% yield along with trimethylsilylbenzene (20%), indicating the effective concentration of **2** to be as 80%.



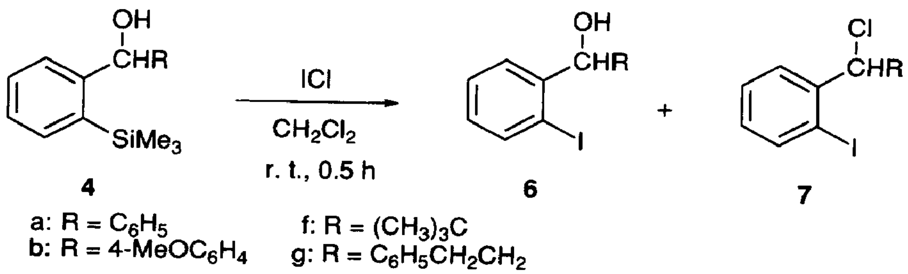
Scheme 1

The reaction of excess **2** with benzaldehyde at -10 °C proceeded cleanly to give benzyl alcohol **4a** in 91% yield (Scheme 1). Reactions of **2** with other aldehydes and ketones are shown in Table 1. The products were identified by means of ^{1}H and ^{13}C NMR and mass spectra. The expected alcohols were obtained in high yields or quantitatively when aromatic aldehydes were used as electrophiles (entries 1-6), whereas the yields in the case of aliphatic aldehydes and ketones were not satisfactory in spite of the apparent cleanliness of the reactions as was witnessed by the absence of by-products from, e. g. aldol-type, side reactions (entries 7-16). As expected, 1,2-addition was shown to be preferred to 1,4-addition when 2-cyclohexenone was used as an electrophile (entry 17). When these reactions were carried out with 1 equivalent of **2** to electrophiles, the yields of the adducts were improved in the case of aldehydes (entries 2, 4, 8, and 11), whereas somewhat reduced yields were obtained in the case of ketones (entries 13 and 15).

Ethyl acetate or acetyl chloride also reacted with **2** to afford **5** and **5'**, however, molar ratio of the reactants did not affect the selectivity of **5** to **5'** (Scheme 2).

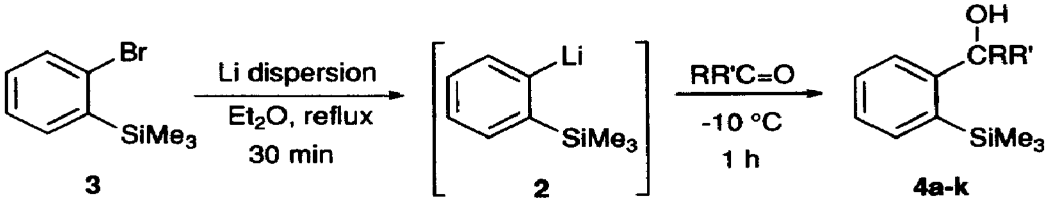


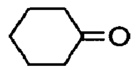
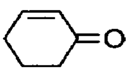
Scheme 2



Scheme 3

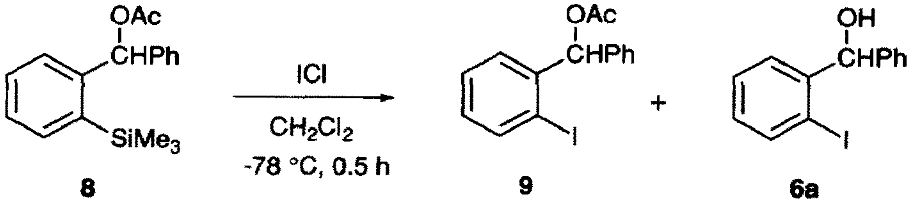
Table 1 Preparation of **4a-k** by the Reaction of **2** with Carbonyl Compounds



entry	electrophiles RR'C=O	equivalent of **2** / eq.	products	yield of **4*** / %
1	PhCHO	2.4	**4a**	91
2		1.0	**4a**	98
3	p-$CH_3OC_6H_4CHO$	2.4	**4b**	99
4		1.0	**4b**	100
5	p-ClC_6H_4CHO	2.4	**4c**	92
6	p-BrC_6H_4CHO	2.4	**4d**	96
7	CH_3CH_2CHO	2.4	**4e**	46
8		1.0	**4e**	63
9	$(CH_3)_3CCHO$	2.4	**4f**	62
10	$Ph(CH_2)_2CHO$	2.4	**4g**	52
11		1.0	**4g**	81
12	$(n$-$C_3H_7)_2CO$	2.4	**4h**	52
13		1.0	**4h**	33
14		2.4	**4i**	66
15		1.0	**4i**	49
16	$PhCOCH_3$	2.4	**4j**	50
17		2.4	**4k**	71

* Isolated yield based on electrophiles.

Direct halogenodesilylation of the adduct **4a** with ICl resulted in a mixture of *o*-iodophenylbenzyl alcohol (**6a**) (50%) and *o*-iodophenylbenzyl chloride (**7a**) (30%), and that of **4b** resulted in quantitative formation of the chloride **7b** (Scheme 3). Similar halogenation of **4f** and **4g** afforded **6f** (74%) and **7f** (23%) and **6g** (46%) and **7g** (23%), respectively. Therefore, we attempted the halogenodesilylation of protected alcohol **8** prepared by the reaction of **2** and benzaldehyde followed by the reaction with acetyl chloride (90% yield). The reaction of **8** with ICl at -78 °C afforded the protected *o*-iodophenyl carbinol **9** (75%) and the carbinol **6a** (25%) (Scheme 4). The acetate, **9**, was hydrolyzed to give **6a** quantitatively.



Scheme 4

Thus, the reaction of **2** with carbonyl compounds followed by halogenodesilylation has been proved to be an effective method for preparing *o*-iodophenylcarbinols, showing the practicability of **2** in reactions in which *o*-iodophenyl anion is formally necessitated.

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