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LITHIUM IODIDE-CATALYZED ALKYLATION OF CARBORANES

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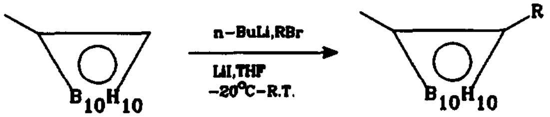
Abstract: The lithium iodide-catalyzed reaction of *o*-carboranyllithium with alkyl bromides yields alkylated *o*-carboranes in excellent yields under very mild conditions.

The synthesis of substituted *o*-carborane derivatives is currently of importance because of their use in boron neutron capture therapy (BNCT).[1] *o*-Carborane derivatives are generally prepared by the reaction of alkynes with decaborane,[2,3] but this route is generally not successful with alkynes that lack an electron withdrawing group.[4]

The alkylation of *o*-carboranyllithium with alkyl bromide usually requires high temperature.[5,6] We wish to report the alkylation of *o*-carboranyllithium with a variety of primary alkyl bromides to produce alkyl *o*-carboranes in excellent yields at low temperatures using lithium iodide as a catalyst. The results are summarized in Table 1 on the next page.

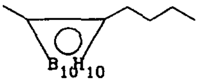
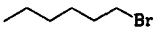
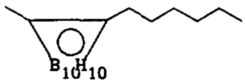
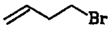
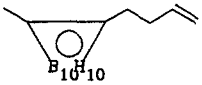
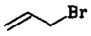
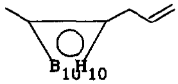
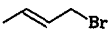
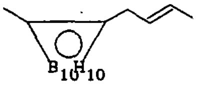
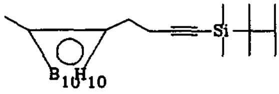
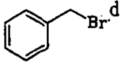
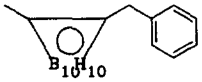


In a typical procedure, *n*-butyllithium (2.5 M in hexanes; 0.48 ml, 1.2 mmol) was added to a solution of methyl-*o*-carborane (158 mg, 1.0 mmol) in dry tetrahydrofuran (10 ml) under an argon atmosphere at 0 °C. The mixture was cooled to -20 °C; lithium iodide[7] (27 mg, 0.2 mmol) in THF (2.0 ml) and alkyl bromide (1.3 mmol) in THF (5.0 ml) were then added and the mixture stirred overnight at ambient temperature. The reaction mixture was quenched with water and the product extracted into ether. The ether layer was washed with water, brine and then dried over $MgSO_4$. Removal of solvent and purification by column chromatography (silica gel; hexanes) furnished the desired product.

4-Bromo-1-butyne (entry 6) failed to react with methyl-*o*-carboranyllithium in the presence of a catalytic quantity of lithium iodide (0.2 eq). Under these conditions, dehydrohalogenation was a competing process leading to the formation of an enyne derivative. Excess lithium iodide (1.2-1.5 eq) was found to be necessary to achieve the desired alkylation.

In conclusion, the lithium iodide catalyzed alkylation of carboranyllithium reagents with alkyl halides was found to be a mild and efficient method for preparing substituted *o*-carboranes in good yields.

TABLE 1. Lithium iodide-catalyzed alkylation of methyl-*o*-carborane

Entry	Alkyl halide	Product[a]	Yield (%)[b]
1			88
2			92
3			94
4			90
5			76
6	[c]		96
7	[d]		89

(a) All products were characterized by IR, NMR and MS Spectra. (b) Isolated yields. (c) An excess of lithium iodide (1.5 eq) was required in this case. (d) Replacement by the chloride led to an 82% yield.

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7. Due to the inherent hygroscopic nature of anhydrous lithium iodide, we chose to prepare our lithium iodide catalyst prior to use. Presumably, freshly opened commercial samples of anhydrous lithium iodide could be utilized successfully.

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