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ALKYLATION OF α,α-DICHLOROARYLMETHANE WITH TRIALKYLBORANES: SYNTHESIS OF ALKYLARYLCARBINOLS

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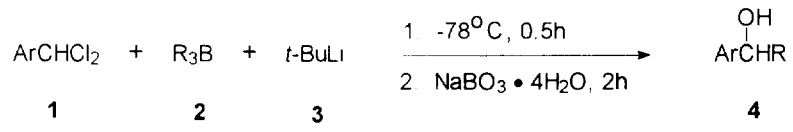
Abstract: The alkylation of α,α-dichloroarylmethane with trialkylboranes occurs readily in the presence of *t*-butyllithium at -78 °C. The reaction affords the corresponding alkylarylcarbinols in good yields after oxidation with sodium perborate.

Alkylation of carbonyl compounds by a reagent such as an organomagnesium, organolithium, or organozinc is one of the most useful reactions in synthetic organic chemistry.[1] However, trialkylboranes, which are easily prepared by the hydroboration of alkenes, generally do not alkylate carbonyl compounds, although a few exceptions are known.[2] Therefore, routes equivalent to the 1,2-addition of an alkyl group from a trialkylborane to a carbonyl group have been developed. Knochel reported that trialkylboranes could first be converted to dialkylzinc reagents via a boron-zinc transmetalation and then the dialkylzinc reagents reacted with carbonyl compounds to generate the 1,2-addition products.[3] We reported that aryl aldehyde tosylhydrazones react with trialkylboranes under basic conditions to generate new trialkylboranes that can be oxidized to produce alkylarylcarbinols.[4] We now wish to report a new reaction of organoboranes, equivalent to the 1,2-addition of trialkylboranes to carbonyl compounds, which involves the reaction of trialkylboranes with dichloroarylmethanes in the presence of *t*-butyllithium.

Aryl aldehydes are easily transformed into dichloroarylmethane derivatives by reaction with phosphorus pentachloride or thionyl chloride.[5] An intermediate α-chloro anion (or aryl carbene) can then be generated from the dichloroarylmethane and trapped by a trialkylborane which produces, after oxidation, the equivalent of a 1,2-addition of an alkyl group of the trialkylborane to an aryl aldehyde. *n*-Butyllithium cannot be used for this purpose, since α,α-dichlorotoluene reacts with *n*-butyllithium to afford α,α-dichlorophenylmethyllithium, which then reacts with alkylboranes to induce the migration of two alkyl groups.[6] However, we have found that a halogen-metal exchange occurs when *t*-BuLi or *s*-BuLi is added to the α,α-dichlorobenzyl reagent. For example, if a molar equivalent of *t*-butyllithium is added to a mixture of α,α-dichlorotoluene and tri-*n*-butylborane in THF at -78 °C, 1-phenyl-1-pentanol

is isolated in 27% yield after oxidation with sodium perborate.[7] The same product is isolated in 21% yield using *s*-BuLi, Scheme 1.

Scheme 1



The reaction conditions were optimized by modifying the molar ratio of the starting substrates, the solvent and the oxidation conditions. The best results were obtained when the reaction was carried out in the THF with a molar ratio of dichloroarylmethane:trialkylborane:*t*-butyllithium of 1:1:2,[8] followed by the oxidation with sodium perborate ($NaBO_3{\cdot}4H_2O$). The reactions of various dichloroarylmethanes with trialkylboranes have been examined, and the results are summarized in Table 1. *n*-Butyldiisopropoxyborane and *n*-butylcatecholborane were also utilized in the reaction. These reagents generated 1-phenyl-1-pentanol in 32% and 36% yield, respectively. The low yields might be due to the decreased electrophilicity of *n*-butyldiisopropoxyborane and *n*-butylcatecholborane when compared to the trialkylboranes. Three major byproducts are generally observed in the reaction. First, lithium trialkylborohydrides form via reaction of the *t*-butyllithium with trialkylboranes;[9] these trialkylborohydrides are detectable by ^{11}B NMR of the reaction mixture prior to oxidation. Second, the nucleophilic substitution of chlorine by *t*-butyllithium to produce $ArCHClC(CH_3)_3$ is observed in all cases; it is the primary reaction when *p*-$CH_3OC_6H_4CHCl_2$ is used (Table 1, entry 7). Third, the reaction intermediates, newly formed trialkylborane containing a substituted benzyl group, are easily protonated under basic conditions.[4] Protonation competes with oxidation using either the perborate or the standard hydrogen peroxide procedure. However, the modified hydrogen peroxide procedure, developed by Brown,[10] can be used to prepare the desired alcohols in difficult cases (Table 1, entry 9).

The reaction presumably occurs via the intermediate formation of an α-chloro anion via a lithium-halogen exchange of a chlorine in the dichloroarylmethane with *t*-butyllithium as outlined in Scheme 2. Good yields of the alkylarylcarbinol are generally obtained.

Scheme 2

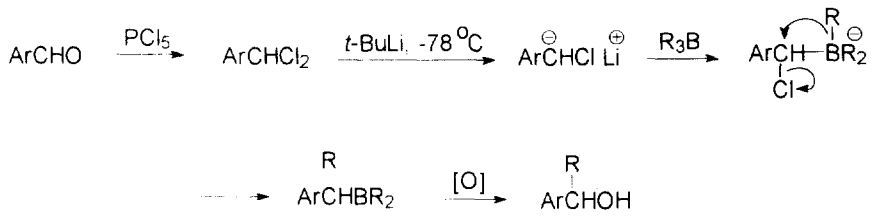


Table 1. Alkylarylcarbinols Prepared

Entry	Product[a]	Ar	R	Yield(%)[b]
1	**4a**	Ph	*n*-Bu	64 (62)[c]
2	**4b**	Ph	*n*-C_6H_{13}	67
3	**4c**	Ph	*n*-C_7H_{15}	62
4	**4d**	Ph	*n*-C_8H_{17}	63
5	**4e**	*p*-ClC_6H_4	*n*-Bu	61
6	**4f**	*p*-$CH_3C_6H_4$	*n*-Bu	63
7	**4g**	*p*-$CH_3OC_6H_4$	*n*-Bu	35[d]
8	**4h**	*m*-$CH_3OC_6H_4$	*n*-Bu	65
9	**4i**	α-naphthyl	*n*-Bu	0[e] (47)[c,f]

[a] All reaction products exhibited physical and spectral characteristics in accord with literature values.

[b] Isolated yield based on dichloroarylmethane.

[c] The yield in parenthesis was obtained using the modified hydrogen peroxide procedure.[10]

[d] A significant amount of *p*-$CH_3OC_6H_4CHClC(CH_3)_3$ was formed (~50%).

[e] 1-Pentylnaphthalene was isolated in 82% yield.

[f] 1-Pentylnaphthalene was isolated in 34% yield.

The synthesis of 1-phenyl-1-pentanol (**4a**) is representative: a mixture of α,α-dichlorotoluene (2.5 mmol, 0.403 g), tri-*n*-butylborane (2.5 mmol, 2.5 mL, 1.0 M solution in THF) and THF (10 mL) was cooled to -78 °C under argon and then *t*-butyllithium (2.5 mmol, 2.94 mL of a 1.7 M solution in pentane) was added to the mixture over a period of approximately 20 min. After the addition was complete, the reaction mixture was stirred at -78 °C for 30 min. and then warmed to 0 °C while maintaining an argon atmosphere. Oxidation was achieved by adding $NaBO_3 \cdot 4H_2O$ (7.5 mmol, 1.15 g) and water (2.5 mL) and stirring the mixture at room temperature for 2h. The product was extracted

into ether (3 x 10 mL), the solvent removed, and the product purified by flash chromatography. 1-Phenyl-1-pentanol (**4a**)[11] was obtained in 64% yield (0.26 g). ^{1}H NMR ($CDCl_3$/TMS) δ: 7.40 - 7.14 (*m*, 5H), 4.60 (*t*, 1H, J = 6.7), 2.19 (*s*, 1H), 1.88 - 1.56 (*m*, 2H), 1.45 - 1.12 (*m*, 4H) 0.97 (*t*, 3H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 144.9, 128.3, 127.4, 125.9, 74.6, 38.8, 27.9, 22.6, 13.9.

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