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Methylphenylborohydride salts and methylphenylborane: new reagents for preparing methylphenylborane derivatives

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Abstract

A new metal borohydride, lithium methylphenylborohydride, was prepared, characterized and used to prepare methylphenylboranes of the type MePhBR.

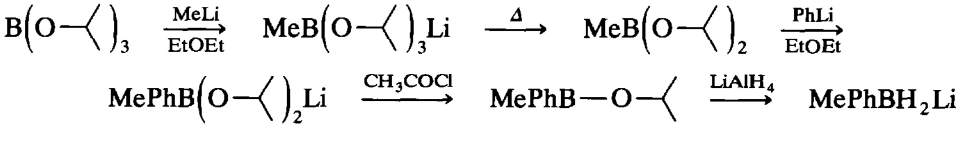
Introduction

The increasing importance of organoboranes as synthetic intermediates has created a need for variety of mixed organoboranes. Organoboranes have been prepared by various methods [1] but only a limited range of mixed triorganylboranes are available owing to the difficulty involved in preparing the prerequisite borane precursors [2], which are often unstable and prone to isomerization and redistribution reactions [3].

We wish to report the synthesis of lithium methylphenylborohydride, a precursor for the synthesis of mixed triorganylboranes containing both the methyl and phenyl groups (Scheme 1).

Results and discussion

Lithium methylphenylborohydride was prepared as outlined in Scheme 1 and characterized by IR (ν(B–H) 2020.42 cm^{-1}) and ^{11}B NMR (−17.16 ppm) spec-



Scheme 1. Preparation of lithium methylphenylborohydride.

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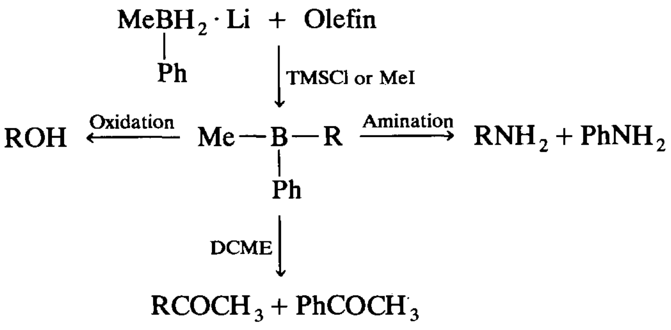


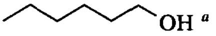
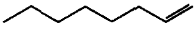
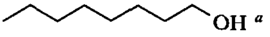
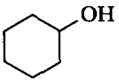
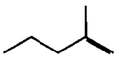
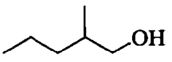
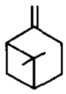
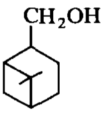
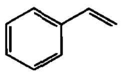
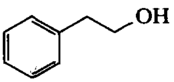
Scheme 2. Generation and reactions of methylphenylborane.

troscopy. The reagent can be stored at 0°C for extended periods of time without decomposition. The reaction of methyl iodide or trimethylsilyl chloride with lithium methylphenylborohydride [4] readily generates free methylphenylborane which, in the presence of alkenes, produces the desired alkylmethylphenylboranes (Scheme 2).

A series of representative alkenes was hydroborated and the regioselectivity of this new hydroborating agent was measured by gas chromatographic analyses of the product alcohols obtained after oxidation. The results are summarized in Table 1. This study revealed that methylphenylborane is a highly regioselective hydroborating agent.

Table 1

Hydroboration-oxidation of alkenes with methylphenylborane

	Alkene	Product	Yield (%) [b]
1			80
2			78
3			76
4			77
5			82
6			85 [c]

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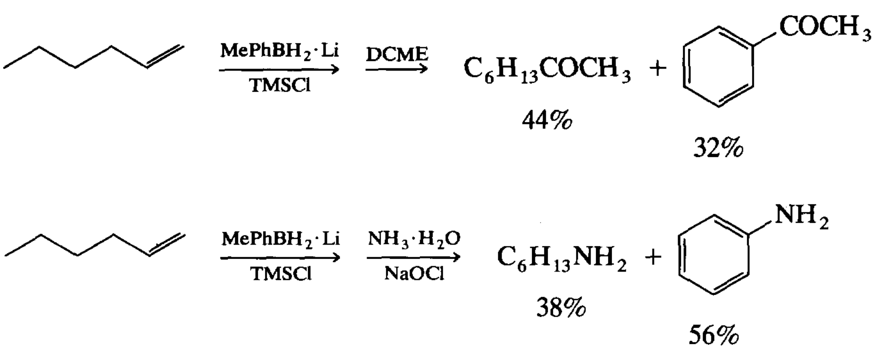
[a] Regioselectivity was greater than 99%. [b] Yields were determined by GLC analysis. [c] Ratio of 1-phenylethanol to 2-phenylethanol was 90 : 10 and the yield reported is the overall yield of the product alcohols.



Scheme 3. The DCME and amination reactions of methylphenylborane.

The stability of lithium methylphenylborohydride was further established by converting it to the methyl borinate ester (MePhBOR) using methanol which, on reaction with dichloromethyl methylether (DCME) [5], produced only methylphenyl ketone in 87% yield. The alkylmethylphenylboranes obtained by hydroboration were also subjected to the DCME and amination [6] reactions (Scheme 3). As anticipated from earlier studies, the phenyl group has a migratory aptitude from boron similar to that of an alkyl group [7].

Experimental

The ^1H and ^{13}C NMR spectra were recorded on a Jeol FX-90Q spectrometer using deuteriochloroform or deuteriomethanol as solvent and the signals are given with reference to TMS. The ^{11}B NMR spectra were recorded using BF_3-etherate as the external reference. Glassware was thoroughly oven-dried and cooled under dry nitrogen just prior to use. Diethyl ether and tetrahydrofuran were dried over calcium hydride and distilled from sodium and benzophenone adduct. Trimethylsilyl chloride, dichloromethyl methyl ether [**CAUTION:** highly toxic lachrymator], alkenes, triethylcarbinol and triisopropylborate (Aldrich Chemical Company) were distilled prior to use. Methyllithium (1.4 *M* solution in cyclohexane), phenyllithium (1.8 *M* solution in cyclohexane), lithium aluminum hydride (1.0 *M* solution in diethyl ether), methyl iodide and sodium percarbonate were used as purchased (Aldrich Chemical Co.). Commercial bleach was used as the source of sodium hypochlorite after determination of its concentration [8]. Lithium triethylcarboxide (1.46 *M* solution in hexane) was prepared from BuLi and triethylcarbinol [5].

Preparation of isopropyl methylboronate

The preparation of isopropyl methylboronate was carried out according to the literature procedure [9] on a 200-mmol scale to yield 27.6 g of the desired product (95.9%, colorless liquid).

Preparation of isopropyl methylphenylborinate

A 500-ml round-bottomed flask, fitted with a septum inlet, was equipped with a magnetic stirring bar, addition funnel, and a gas outlet connected to a mercury bubbler. Isopropyl methylboronate (106 mmol, 15.3 g) was placed in the flask via a syringe followed by diethyl ether (120 ml). The solution was cooled to −78°C (dry ice–acetone bath). Phenyllithium (106 mmol, 59.0 ml of a 1.8 *M* solution in cyclohexane) was added dropwise over a period of 25 min. After the addition was complete, the reaction mixture was stirred at −78°C for 4 h, warmed to 0°C, and stirred for an additional hour; acetyl chloride (106 mmol, 8.33 g) was then added dropwise via syringe. During the addition, a white precipitate formed; the ice bath was removed after the addition and the mixture stirred at room temperature for 20 min.

A separate nitrogen-flushed 500-ml round-bottomed flask equipped with a septum inlet, magnetic stirring bar, and a sintered glass fritted funnel fitted with a septum cap was assembled while hot. The reaction mixture was then filtered under nitrogen by transferring it into the fritted funnel using a 12 gauge double-ended needle. After washing the precipitate with dry ether (2 × 75 ml), the solvent was removed from the filtrate by slow distillation under nitrogen. The residue was distilled under vacuum to yield the desired product (14.2 g, 82.8%) as a colorless liquid: b.p. 44–47°C (5 mmHg). ^{1}H NMR ($CDCl_3$): 7.57 (m, 2H); 7.30 (m, 3H); 4.57 (septet, 1H); 1.25 (d, 6H); 0.72 (s, 3H) ppm. ^{13}C NMR: 133.9, 130.8, 127.5, 68.0, 24.6 ppm. ^{11}B-NMR: 47.5 ppm.

Preparation of lithium methylphenylborohydride

A 250-ml round-bottomed flask fitted with a septum inlet and equipped with a magnetic stirring bar and a gas outlet connected to a mercury bubbler was flame dried, and cooled to −5°C under a stream of argon. Dry diethyl ether (50 ml) and isopropyl methylphenylborinate (50 mmol, 8.2 g) were introduced into the flask followed by the slow addition of cold (0°C) lithium aluminum hydride (50 mmol, 50 ml of a 1 *M* solution in diethyl ether). The mixture was stirred at −5°C for 5 min and then warmed to room temperature and stirred for 30 min. The solution was recooled to −5°C and triethylenediamine in ether (25 mmol, 2.8 g in 40 ml of ether) was slowly added. A white precipitate of bis(monoisopropylalane)-triethylenediamine complex instantly formed. The reaction mixture was stirred vigorously at 25°C for 15 min and then the precipitate was allowed to settle overnight.

A separate apparatus consisting of a 250-ml round-bottomed flask fitted with a septum inlet, magnetic stirring bar, and a sintered glass fritted funnel capped with a septum was assembled, flame-dried and cooled to 0°C under a stream of argon. The lithium methylphenylborohydride solution was filtered under argon through the filter funnel by using a double-ended needle. The precipitate was washed with ether (2 × 15 ml). The borohydride solution (in diethyl ether) was analyzed by ^{11}B NMR spectroscopy which revealed a signal at −17.2 ppm and an IR absorbance at 2070.42 cm^{-1}. The hydride analysis established the yield at 98% [10].

General procedure for the hydroboration of alkenes

In a reaction flask fitted with a thermometer, magnetic stirring bar, and septum capped-side arm connected to a mercury bubbler, were placed dry ether (10 ml) and lithium methylphenylborohydride (5.0 mmol, 10.4 ml of a 0.48 *M* solution). The flask was cooled to −5°C and 1-hexene (0.42 g, 5.0 mmol) was added; this was followed by the dropwise addition of trimethylsilyl chloride (0.60 g, 5.5 mmol). A white precipitate was formed during the exothermic reaction. The reaction mixture was stirred at −3°C for 0.5 h and then at room temperature for 1 h. A ^{11}B NMR spectrum of methylphenylalkylboranes revealed resonances between 84 and 85.5 ppm.

Representative oxidation

To a hexylmethylphenylborane (5.0 mmol) solution prepared as described above, ethanol (10 ml) was added followed by water (10 ml) and sodium percarbonate (23 mmol, 3.5 g) [11]. The reaction mixture was stirred at 50°C for 1 h to ensure complete oxidation. After cooling, the product was extracted into ether (3 × 25 ml) and the combined organic layer washed with aqueous NaOH (10 ml) to remove the phenol. The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure. 1-Heptanol was added as an internal standard and the yield of 1-hexanol was determined by GLC (yield 80%). The regioselectivity was found to be greater than 99%.

Representative DCME reaction

To a hexylmethylphenylborane (5.0 mmol) solution prepared as described above, dichloromethyl methyl ether (1.15 g, 10.0 mmol) [CAUTION: highly toxic lachrymator] was added followed by the addition of lithium triethylcarboxide (10.0 mmol, 6.85 ml of a 1.46 *M* solution in hexane) at 0°C over a period of 10 min. The mixture was stirred at 0°C, for 0.5 h and then at room temperature for 2 h. Ethylene glycol (3 ml) was added followed by the addition of THF (15 ml) and sodium hydroxide (1.2 g). Oxidation was accomplished by the slow addition of hydrogen peroxide (4 ml, 30% solution) at 0°C followed by warming to ~ 60°C for 1 h. The aqueous and organic phases were separated and the aqueous phase was extracted with ether (3 × 25 ml). The combined organic layer was washed with brine, dried ($MgSO_4$), and the solvent removed under reduced pressure. The crude product was chromatographed (silica gel, hexane) to yield 2-octanone (0.288 g, 45%) and acetophenone (0.19 g, 32%).

Representative amination reaction

The hexylmethylphenylborane (5.0 mmol) solution prepared as described above was cooled to 0°C under an argon atmosphere and ammonium hydroxide (5.5 mmol, 2.85 ml of a 1.93 *N* solution) was added followed by the dropwise addition of aqueous sodium hypochlorite (6.5 mmol, 8.84 ml of a 0.735 *M* solution). The solution was allowed to warm to 25°C and then stirred for 0.5 h. The solution was acidified to pH 1 (10% HCl) and washed with ether. The amines were regenerated from their hydrochlorides via neutralization of the aqueous layer using 6 *N* NaOH; they were extracted into ether (3 × 25 ml). The ether layer was dried over solid KOH and the solvent removed under reduced pressure; the crude product was distilled initially at atmospheric pressure to isolate hexylamine (0.19 g, 38%) and then under reduced pressure to isolate aniline (0.2 g, 56%). The products exhibited physical and spectral properties in accord with authentic samples.

Acknowledgement

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