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Evidence for the Formation of Acylboronate Intermediates in the Carbonylation Reactions of Organoboranes

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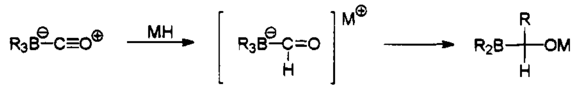
Summary: Trialkylboranes react with acyllithium reagents to yield ketones after oxidation with hydrogen peroxide. The ketones contain one alkyl group supplied by the alkyllithium reagent and one alkyl group supplied by the organoborane. The experimental results support the hypothesis that an acylboronate is an intermediate in the reactions of organoboranes with carbon monoxide. The yields are modest due to an apparent competition between carbon monoxide and organoborane for the alkyllithium needed to generate the acyl anion.

Background

The reaction of carbon monoxide with trialkylboranes has proven to be an important addition to the carbon−carbon bond forming methodologies available to the synthetic chemist.[1] One, two, or three alkyl groups can be transferred from boron to the carbon of carbon monoxide depending upon whether metal hydrides,[2] water,[3] or high reaction temperatures[4] are utilized during the carbonylation. The scope of this process is broad, allowing access to aldehydes, ketones, and carbinols.[5] The organoborane carbonylation reactions all presumably proceed via the intermediate formation of acylborane or acylboronate complexes.[6] Interestingly, the organoborate complexes should be available via the direct reaction of an acyl anion (RCO^-M^+) with an organoborane. However, due to the general unavailability of acyl anions, no reports have appeared in the literature concerning the interception of these species by organoboranes. An early report concerning the synthesis of an acylborane prepared by sequential treatment of dibutylmonochloroborane with sodium−potassium alloy and benzoyl chloride[7] was later shown to be erroneous.[8]

Introduction

The mechanism of the hydride-induced carbonylation reaction is presumed to involve an acylboronate intermediate, **1** (eq 1). This hypothesis is based on the nature of the observed products and the studies carried out by Hubbard.[9] We wish to report evidence for the veracity of the acylboronate intermediate based upon the products isolated from the reaction of trialkylboranes with acyl anions.



$$R_3\overset{\ominus}{B}-C\equiv O^{\oplus} \xrightarrow{MH} \left[R_3\overset{\ominus}{B}-\underset{H}{C}=O\right]M^{\oplus} \longrightarrow R_2B-\underset{H}{\overset{R}{\vert}}-OM \quad (1)$$

1

Seyferth has reported the reaction of various electrophiles with acyllithium anions (RCOLi) generated by the reaction of carbon monoxide with alkyl- and aryllithiums at −110 to −135 °C.[10] The reaction of these acyl anions with a Lewis acid such as an organoborane (eq 2) should offer a direct route to the acylboronate complex analogous to that proposed in the carbonylation mechanism.

(2)

Indeed, subjecting trialkylboranes to acyllithium reagents generated *in situ* by the Seyferth method, followed by an alkaline hydrogen peroxide oxidative workup, results in the formation of ketones (eq 3). The resulting ketones contain one alkyl group supplied by the alkyllithium reagent and one alkyl group supplied by the organoborane.

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[1] (a) Reppe, W.; Magin, A. German Patent 1076130, 1960; *Chem. Abstr.* **1961**, *55*, P10386i. (b) Hillman, M. E. D. *J. Am. Chem. Soc.* **1962**, *84*, 4715. (c) Hillman, M. E. *J. Am. Chem. Soc.* **1963**, *85*, 982, 1626. (d) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1967**, *89*, 5477. (e) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1967**, *89*, 5285. (f) Negishi, E.; Brown, H. C. *Synthesis* **1972**, 196.

[2] (a) Brown, H. C.; Coleman, R. A. *J. Am. Chem. Soc.* **1969**, *91*, 4606. (b) Brown, H. C.; Knights, E. F.; Coleman, R. A. *J. Am. Chem. Soc.* **1969**, *91*, 2144. (c) Brown, H. C.; Hubbard, J. L.; Smith, K. *Synthesis* **1979**, 701.

[3] Brown, H. C.; Rathke, M. W. *J. Am. Chem. Soc.* **1967**, *89*, 2737.

[4] Brown, H. C.; Rathke, M. W. *J. Am. Chem. Soc.* **1967**, *89*, 4528.

[5] (a) Reichert, C. F.; Pye, W. E.; Bryson, T. A. *Tetrahedron* **1981**, *37*, 2441. (b) Bryson, T. A.; Pye, W. E. *J. Org. Chem.* **1977**, *42*, 3214. (c) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1969**, *91*, 1224. (d) Brown, H. C.; Negishi, E. *Chem. Commun.* **1968**, *594*. (e) Hubbard, J. L.; Brown, H. C. *Synthesis* **1978**, 676. (f) Brown, H. C.; Ford, T. M.; Hubbard, J. L. *J. Org. Chem.* **1980**, *45*, 4067.

[6] (a) Brown, H. C. *Acc. Chem. Res.* **1969**, *2*, 65. (b) Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: New York, 1988; pp 274−280. (c) Brown, H. C.; Negishi, E.; Dickason, W. C. *J. Org. Chem.* **1985**, *50*, 520. (d) Srebnik, M.; Cole, P. E.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1989**, *54*, 6085.

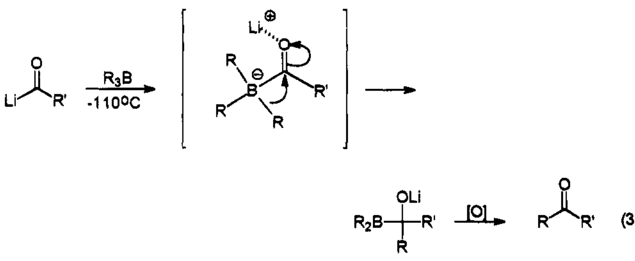
[7] Schmid, G.; Nöth, H. *Chem. Ber.* **1968**, *101*, 2502.

[8] Smith, K.; Swaminathan, K. *J. Chem. Soc., Chem. Commun.* **1975**, 719.

[9] (a) Brown, H. C.; Hubbard, J. L. *J. Org. Chem.* **1979**, *44*, 467. (b) Brown, H. C.; Krishnamurthy, S.; Coleman, R. A.; Hubbard, J. L. *J. Organomet. Chem.* **1979**, *166*, 281. (c) Hubbard, J. L.; Smith, K. *J. Organomet. Chem.* **1984**, *276*, C41. (d) Hubbard, J. L. *Heteroatom. Chem.* **1992**, *3*, 223. (e) Hubbard, J. L. *J. Organomet. Chem.* **1993**, *445*, 7.

[10] (a) Seyferth, D.; Weinstein, R. M. *J. Am. Chem. Soc.* **1982**, *104*, 5534. (b) Seyferth, D.; Weinstein, R. M.; Wang, W.-L. *J. Org. Chem.* **1983**, *48*, 114. (c) Weinstein, R. M.; Wang, W.-L.; Seyferth, D. *J. Org. Chem.* **1983**, *48*, 3367. (d) Seyferth, D.; Weinstein, R. M.; Wang, W.-L.; Hui, R. C. *Tetrahedron Lett.* **1983**, *24*, 4907. (e) Seyferth, D.; Hui, R. C. *Organometallics* **1984**, *3*, 327. (f) Seyferth, D.; Wang, W.-L.; Hui, R. C. *Tetrahedron Lett.* **1984**, *25*, 1651. (g) Seyferth, D.; Hui, R. C. *Tetrahedron Lett.* **1984**, *25*, 2623, 5251. (h) Seyferth, D.; Hui, R. C. *J. Org. Chem.* **1985**, *50*, 1985. (i) Seyferth, D.; Weinstein, R. M.; Hui, R. C.; Wang, W.-L.; Archer, C. M. *J. Org. Chem.* **1991**, *56*, 5768. (j) Seyferth, D.; Weinstein, R. M.; Hui, R. C.; Wang, W.-L.; Archer, C. M. *J. Org. Chem.* **1992**, *57*, 5620.

0276-7333/94/2313-5163$04.50/0



(3)

Results and Discussion

Very low temperatures (i.e., −115 °C) are necessary for production of the lithium-stabilized acyl anions which are generated by addition of an alkyllithium species to a carbon monoxide-saturated solution. Seyferth's studies indicate that the acyl anion can be generated either prior to addition of, or in the presence of, an electrophile. In Seyferth's system, reaction of the organolithium with carbon monoxide (presumably an electron transfer process)[11] is fast compared with alkylation of the electrophiles investigated. However, organoboranes readily react with organolithium reagents to form stable organoborates at −115 °C.

Three procedures were examined in an effort to optimize the reaction of acyl anions with organoboranes. First, as shown in Table 1 (entry 2), the acyl anion was generated from *n*-butyllithium at −115 °C in the presence of the tributylborane. As expected, the acyl anion reacted with the trialkylborane which was followed by the migration of one alkyl group from boron to carbon to give, upon oxidation, 5-nonanone. However, the predominant formation of tetrabutylboronate demonstrates that the organoborane effectively competes with carbon monoxide for the alkyllithium. In fact, the tetraorganoborate complex was found to be the major product under all reaction conditions. Attempts to preform the acyl anion (as evidenced by the appearance of a pronounced deep red color) followed by the addition of the trialkylborane (method B) failed to increase the yield of ketone (entries 15−17). Finally, the simultaneous addition (method C) of alkyllithium and trialkylborane to carbon monoxide (entries 18−20) gave results comparable to those obtained utilizing method B.

The reaction temperature was found to be of major importance (entries 2−5, 15−16). Presumably, at higher temperatures the acyl anion is relatively unstable; this enhances the rate of side reactions such as dimerization. The concentration of the reactants also appears to be important. Using methods A or B, an increase in reactant concentration reduced the yield of product ketone (entries 6 and 17). Method C, as would be anticipated, was unaffected (entry 19).

In an attempt to moderate the electrophilicity of the organoborane and slow the formation of the tetraalkylborate, Lewis bases such as triethylamine (entries 7−10, 20), triphenylphosphine (entries 12−13), and dimethyl sulfide (entry 11) were added to the reaction mixture.[12] The yield of ketone was unaffected. However, the addition of the crown ether, 18-crown-6 (entry 14), led to somewhat higher yields.

The reaction of tributylborane with the acyl anion generated from butyllithium was used in the preliminary experiments. The acyl anion was shown to be the source of one of the alkyl groups, and the organoborane the other, in two ways. First, it was confirmed that conventional carbonylations do not occur at low temperatures by bubbling carbon monoxide through a solution containing only tributylborane and verifying that no carbonylation products were formed (Table 1, entry 1). In a separate set of experiments (Table 2), carbon monoxide was bubbled through a solution of *n*-butyllithium at −115 °C followed by the addition of trioctylborane. Upon oxidation, the expected 5-tridecanone was isolated. These experiments unambiguously demonstrate that the alkyl groups in the product ketone are supplied by both the alkyllithium reagent and the triorganoborane.

Table 1. Formation of 5-Nonanone via Reaction of Tributylborane with Butyllithium and Carbon Monoxide

expt no.	method	[R$_3$B], mM	base	temp, °C	% yield
1	control^a	0.033		−115	0
2	A	0.033		−115	18
3	A	0.033		−78	6
4	A	0.033		−10	5
5	A	0.033		0	4
6	A	0.066		−115	0
7	A	0.033	Et$_3$N^b	−115	18
8	A	0.033	Et$_3$N^c	−115	9
9	A	0.033	Et$_3$N^d	−115	9
10	A	0.033	Et$_3$N^e	−115	11
11	A	0.033	Me$_2$S^b	−115	10
12	A	0.033	Ph$_3$P^b	−115	17
13	A	0.033	Ph$_3$P^e	−115	9
14	A	0.033	18-crown-6^f	−115	21
15	B	0.033		−115	10
16	B	0.033		−78	2
17	B	0.066		−115	3
18	C	0.033^g		−115	8
19	C	0.066^g		−115	8
20	C	0.033^g	Et$_3$N^c	−115	9

[a] No BuLi added. [b] 1 molar equiv of base added prior to borane and butyllithium addition. [c] 1 molar equiv of base complexed with borane prior to addition. [d] 2 molar equiv of base added prior to borane and butyllithium addition. [e] 10 molar equivalent of base added prior to borane and butyllithium addition. [f] 2 mol %. [g] Maximum possible final concentration.

Table 2. Reaction of Trioctylborane with *n*-BuLi and CO

entry	[R$_3$B], mM	time, h	% yield	method
1	0.033	1	18	A
2	0.033	1	10	B
3	0.033	1	9	C

Conclusion

The production of ketone products via the reaction of acyl anions with organoboranes supports the hypothesis that an acylboronate is an intermediate in the organoborane carbonylation reactions. Although the existence of the acylboronate is supported only by indirect evidence, all other routes by which the product ketone could have formed have been eliminated.

Experimental Section

All reagents and solvents were transferred using techniques designed to eliminate contact with the atmosphere. Glassware and syringes were oven-dried for 24 h prior to use. THF and diethyl ether were distilled from benzophenone ketyl. Pentane was distilled from calcium hydride. Tributylborane (Callery Industries) was used as received. Butyllithium (Aldrich, 1.6 M in hexanes) was standardized by titration with 1-butanol

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(11) Nudelman, N. S.; Doctorovich, F.; Amorin, G. *Tetrahedron Lett.* **1990**, *31*, 2533 and references cited therein.

(12) Addition of unhindered amines such as trimethylamine or pyridine resulted in complete inhibition of the reaction.

using 1,10-phenanthroline as an indicator.[13] All other reagents were reagent grade and utilized as received.

Product analyses were performed by GC and GC/MS using, respectively, a Varian Model 3700 gas chromatograph with flame ionization detection and an HP Model 5890A gas chromatograph fitted with a quadrupole mass spectrometric detector. Yields were determined by comparison with an internal standard (tetradecane). TLC was performed on silica plates (Analtech); compounds were visualized using phosphomolybdic acid (5% in ethanol) as a staining agent.

The temperature of the reaction mixture was monitored using an electronic thermometer equipped with a thermocouple. The thermocouple wire was contained within a glass tube filled with pentane to prevent contamination of the reaction mixture. The low temperatures needed for the reaction were obtained by immersing the reaction flask in a slurry of 1-propanol and liquid nitrogen.

Three reaction protocols were utilized to evaluate the low-temperature reaction. The first involved formation of the acyl anion in the presence of the organoborane, the second involved preformation of the acyl anion followed by addition of the organoborane, while the third utilized simultaneous formation of the acyl anion and addition of the organoborane. Detailed procedures are presented below.

Method A. To a three-necked, 250 mL, round bottomed flask equipped with magnetic stirrer, glass-enclosed thermocouple probe, a side arm fitted with a rubber septum, and a fritted-glass gas dispersion tube was added 150 mL of a 4:4:1 mixture of THF, diethyl ether, and pentane. The solvent mixture was cooled to −115 ± 5 °C by immersion of the flask in a low-temperature bath. Carbon monoxide was then bubbled into the solvent for 30 min prior to, and throughout, the introduction of the reagents. The organoborane (5 mmol, 5 mL of a 1 M solution in THF) was then added, followed by the dropwise introduction of the alkyllithium solution (5 mmol, 3.1 mL of a 1.6 M solution) via syringe over a period of approximately 20 min, forming a pale yellow solution. After the addition was complete, the reaction was stirred at −115 °C for 1 h and then allowed to warm to room temperature. After warming to 0 °C, an excess of 30% hydrogen peroxide (2 mL) and 3.0 M NaOH (2 mL) were added to oxidize the organoborane intermediates. The solution was heated to reflux for approximately 1 h, cooled, and concentrated by rotary evaporation, and the yellowish residue was taken up into hexane. The hexane solution was washed with water, saturated sodium bicarbonate, and brine. The organic fraction was then dried over anhydrous magnesium sulfate, filtered, and concentrated. The product was initially isolated by flash chromatography and exhibited physical and spectral characteristics in accord with an authentic sample. Subsequent reactions were characterized by gas chromatographic analyses.

Method B. This procedure was identical to that described for method A except that the organoborane was added after the addition of the alkyllithium to the carbon monoxide-saturated solution was complete. A deep red color was observed upon addition of the alkyllithium, but this dissipated upon the dropwise addition of the organoborane over a period of 20 min.

Method C. The third procedure was identical to the first except that the organoborane and alkyllithium were added simultaneously over a period of 20 min.

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[13] Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.