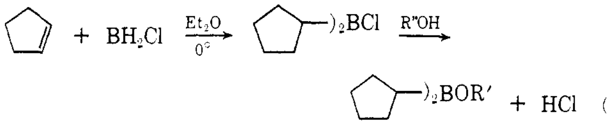
Base-Induced Reaction of Borinic Acid Esters with α,α-Dichloromethyl Methyl Ether. A New Route to Ketones *via* Hydroboration

Sir:

Esters of borinic acids are transformed under exceptionally mild conditions by α,α-dichloromethyl methyl ether (DCME) and lithium triethylcarboxide into an intermediate which can readily be oxidized to the corresponding ketone in high yields (eq 1). Dialkylborinates are now readily available *via* hydroboration of the respective olefins with monochloroborane etherate followed by alcoholysis of the product[1] (eq 2). Consequently, this procedure provides a new versatile route from olefins to ketones *via* hydroboration.

$$R_2BOR' + CHCl_2OCH_3 + LiOCEt_3 \xrightarrow[0.5\ \text{hr}]{\text{THF, }25°} [\quad] \xrightarrow[\text{NaOH}]{H_2O_2} R_2CO \qquad (1)$$



(2)

The reactions of trialkylboranes with carbon monoxide in the presence of water[2] or with sodium cyanide and trifluoroacetic anhydride[3] provide valuable new routes to ketones. The loss of one of the three alkyl groups in this synthesis can be circumvented by utilizing the thexyldialkylboranes.[4,5] Unfortunately, the synthesis of thexyldialkylboranes with two highly hindered alkyl groups offers difficulties.[6]

We recently established a simple synthetic route to dialkylchloroboranes and the corresponding esters[1] (eq 2). This procedure readily accommodates even very bulky alkyl groups. Unfortunately, such borinic esters fail to react with carbon monoxide[7] or with sodium cyanide and trifluoroacetic acid anhydride.[8] Our recent success in converting organoboranes into the corresponding carbinols, by the base-induced reaction with DCME under exceptionally mild conditions,[9] even in the case of highly hindered organoboranes,[10] led us to explore this route. Indeed, conditions were found under which the reaction proceeds simply and cleanly, yielding the corresponding ketone in excellent yield (eq 1).

We noted previously that only 1 equiv of base was required in the reaction of DCME and trialkylboranes for complete conversion to trialkylcarbinols. The more sterically open methyl esters of dialkylborinic acids, however, generally require 2 equiv of base for complete conversion to the corresponding ketones. Apparently even the moderately hindered base, lithium triethylcarboxide, can competitively coordinate with the boron atom in these cases. As the steric environment around boron becomes more crowded, the yields of ketone with 1 equiv of the base rise sharply. This effect is evident in the results summarized in Table I.

Table I. Preparation of Ketones *via* the Reaction of Methyl Borinates with DCME and Lithium Triethylcarboxide

Methyl borinate (R_2BOMe) R =	Ketone	Yield of ketone, %[a] 1 equiv of base	2 equiv of base
n-Butyl	5-Nonanone	35	96
Isobutyl	2,6-Dimethyl-4-heptanone	56	86
sec-Butyl	3,5-Dimethyl-4-heptanone	72	80[b]
Cyclopentyl	Dicyclopentyl ketone	59	86[c]
Cyclohexyl	Dicyclohexyl ketone	95 (85)[d]	
3-Methyl-2-butyl	2,3,5,6-Tetramethyl-4-heptanone	41	54 (42)[e]
exo-2-Norbornyl	Bis(*exo*-norbornyl) ketone	62 (53)[f]	
trans-2-Methylcyclopentyl	Bis(*trans*-2-methylcyclopentyl) ketone	83 (80)[g]	

[a] Yields by glpc analysis. [b] Accompanied by ~10% of a side product, identified as the internal olefin, R=CHR, presumably from elimination in the α-chloroborinate intermediate. [c] Approximately 10% of an olefinic side product, as in footnote *b*. [d] Product isolated by distillation, bp 96–98° (1.2 mm), n^{20}D 1.4838. [e] Product isolated by distillation, bp 142–144° (210 mm), n^{20}D 1.4305. Accompanied by ~30% of internal olefin. [f] Product purified by column chromatography, mp 53–54°. Also produced was 29% of the internal olefin, identified as *exo*-norbornylmethylene-2-norbornane. [g] Product purified by distillation, bp 62–63° (0.6 mm), n^{20}D 1.4693 (A. Pelter, M. G. Hutchings, and K. Smith, *J. Chem. Soc., Chem. Commun.*, 186 (1973)).

In cases such as methyl di-*n*-butylborinate where the alkyl groups provide little steric protection of the boron, competitive coordination of the base can be reduced by using a bulkier ester group. These can be conveniently prepared by treating the dialkylborane or the dialkylchloroborane with the desired alcohol or phenol. In such cases, the yield achieved with only 1 equiv of base increases sharply. For example, whereas the methyl ester of di-*n*-butylborinate gives a 35% yield with 1 equiv of base, the corresponding 2,6-dimethylphenyl ester provides a yield of 87% of 5-nonanone. Representative results are summarized in Table II.

Table II. Reaction of Alkyl and Aryl Esters of Di-*n*-butylborinic Acid with DCME and One Equivalent of Lithium Triethylcarboxide

Ester, *n*-Bu_2BOR' R′ =	Yield of 5-nonanone, %[a]
Methyl	35
n-Butyl	44
tert-Butyl	57
Triethylcarbinyl	64
Phenyl	31
2,6-Dimethylphenyl	87
2,6-Diisopropylphenyl	80

[a] Glpc analyses.

The results realized in the synthesis of bis(*exo*-norbornyl) ketone and bis(*trans*-2-methylcyclopentyl) ketone (Table I) establish that the transfer of alkyl groups from boron to carbon in the present reaction

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[1] H. C. Brown and N. Ravindran, *J. Amer. Chem. Soc.*, **94**, 2112 (1972).

[2] H. C. Brown and M. W. Rathke, *ibid.*, **89**, 2738 (1967).

[3] A. Pelter, M. G. Hutchings, and K. Smith, *Chem. Commun.*, 1529 (1970).

[4] H. C. Brown and E. Negishi, *J. Amer. Chem. Soc.*, **89**, 5285 (1967).

[5] A. Pelter, M. G. Hutchings, and K. Smith, *Chem. Commun.*, 1048 (1971).

[6] C. F. Lane and H. C. Brown, *J. Organometal. Chem.*, **34**, C29 (1972).

[7] Unpublished research of E. F. Knights.

[8] Private communication from A. Pelter.

[9] H. C. Brown and B. A. Carlson, *J. Org. Chem.*, **38**, 2422 (1973).

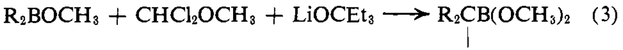
[10] H. C. Brown, J.-J. Katz, and B. A. Carlson, *J. Org. Chem.* in press.

proceeds with retention of configuration at the migrating carbon. Such retention has been previously established for carbonylation[11] and for the cyanoborate reaction.[12] Consequently, in combination with the remarkable characteristics of the hydroboration reaction these procedures provide highly valuable methods for assembling carbon structures in a stereospecific manner with the aid of boron.

The following procedure is representative. A dry 500-ml flask, fitted with a septum inlet, magnetic stirrer, and reflux condenser, was flushed with nitrogen and maintained under a static pressure of the gas. In this flask was placed 19.6 ml of a 2.55 *M* solution of borane (50 mmol) in THF and 20.0 ml of THF. An ice bath was placed about the flask and 9.6 g (100 mmol) of cyclohexene was added. After 1 hr at 0°, 1.6 g (50 mmol) of methanol was added slowly to form the ester, methyl dicyclohexylborinate. To the reaction mixture was added 5.0 ml (6.53 g) (~10% excess) of DCME, followed by 25.4 ml of a 1.97 *M* solution of lithium triethylcarboxide (50 mmol) in hexane over 5 min. (The base was prepared from *n*-butyllithium and triethylcarbinol.) The reaction mixture was allowed to come to room temperature and maintained there for 0.5 hr. A heavy white precipitate, presumably lithium chloride, was observed. Then 20 ml of 95% ethanol was added, followed by 4 g of sodium hydroxide and 15 ml of 30% hydrogen peroxide (slow!). The oxidation mixture was cautiously heated and maintained at 50–60° for 1 hr to complete the oxidation. The aqueous phase was separated by saturation with sodium chloride. Distillation of the dry tetrahydrofuran phase yielded 8.2 g of dicyclohexyl ketone: bp 96–98° (1.2 mm); $n^{20}\text{D}$ 1.4838; yield, 85%.

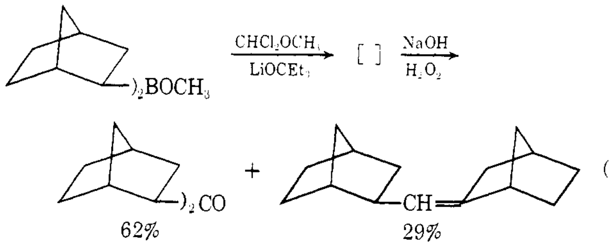
The hydroboration of cyclohexene, methylcyclopentene, and 3-methyl-2-butene can be controlled to yield the dialkylborane, readily convertible to the methyl borinates by treatment with methanol, as in the above procedure. All other olefins were converted to the dialkylchloroboranes by hydroboration with monochloroborane diethyl etherate,[1] and the latter was converted to the methyl esters by treatment with 100% excess methanol at 0° for 0.25 hr. The excess methanol, diethyl ether, and hydrogen chloride were removed under reduced pressure with an aspirator, THF was added to make a solution, ~1 *M*, and the reaction with DCME was carried out as above.

The intermediate in this base-induced reaction of methyl dialkylborinates with DCME has been identified as an α-chloroboronate[13] (eq 3). It was observed that



$$R_2BOCH_3 + CHCl_2OCH_3 + LiOCEt_3 \longrightarrow R_2\underset{\displaystyle Cl}{\underset{|}{C}}B(OCH_3)_2 \quad (3)$$

in some cases involving secondary alkyl groups there was formed, in addition to the ketone, small to moderate amounts of internal olefins.[14] These apparently arise from a competing elimination reaction of the intermediate. For example, methyl bis(*exo*-norbornyl)-borinate produced 62% of bis(*exo*-norbornyl) ketone and 29% of *exo*-norbornylmethylene-2-norbornane (eq 4). This side reaction promises to provide a valuable new route to such olefins.



(4)

The present procedure provides a facile route from olefins to ketones. It appears to be of wide generality accommodating even bulky groups without apparent difficulty. It makes evident still another fascinating facet of the remarkable chemistry of organoboranes.

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[11] H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *J. Amer. Chem. Soc.*, **91**, 2150 (1969).

[12] See Pelter, *et al.*, footnote *g*, Table I.

[13] For example, the α-chloroboronate in the representative reaction above was isolated prior to the oxidation in 82% yield. It was identified by nmr, ir, mass spectral, and elemental analysis.

[14] A similar phenomenon has been observed in the cyanoborate reaction: M. G. Hutchings, Ph.D. Thesis, University of Manchester.

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Book Reviews

Physical Methods of Chemistry. Part III.D. Edited by A. WEISSBERGER and B. W. ROSSITER (Eastman Kodak Co.). Wiley-Interscience, New York, N. Y. 1972. xiv + 705 pp. $32.00.

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