addition products has been ruled out by the observation that the lithium salt of **3** is unchanged by *t*-butyllithium, either by itself or in the presence of a functioning epoxide reaction. The fact that olefin formation is not as important for those epoxides which undergo facile carbenoid reactions is suggestive that a related carbenoid mechanism is also operative for eq 1. Thus, metalation at an epoxide ring carbon produces the organolithium intermediate **4**. This species can undergo α elimination and carbenoid insertion into the carbon–lithium bond of a second *t*-butyllithium molecule to give **6**. This unusual chemical entity is proposed to *spontaneously eliminate the elements of lithium oxide*, thereby generating the olefinic bond of **2**. This description is an oversimplification, since it is well known that alkyllithiums exist as monomer aggregates in hydrocarbon solvents and that these units are modified by coordination with Lewis bases such as ethers (epoxides) and alkoxides.[6] However, it is not profitable to pursue this complicating factor for the present except to note that the carbenoid insertion into the carbon–lithium bond is therefore essentially an intramolecular event. Current knowledge[7] suggests that the α-elimination–insertion process is concerted and probably by-passes the free carbene stage.

The mechanistic sequence shown above is well precedented and relatively unexceptional, save for the last step involving loss of lithium oxide. The driving force for this elimination from **6** is thought to derive from the exceptionally high heat of formation of the metal oxide (142 kcal/mole).[8] We believe that the loss of stable metal oxides (Li, Al, B, etc.) may well prove to be a general reaction for species such as **6**, which have a metal and a metal alkoxide bonded to vicinal carbon atoms. The gross details of certain lithium aluminum hydride reductions of metal salts of β-dicarbonyl compounds to yield allylic alcohols[9] and the reactions of geminally dimetalated alkanes with carbonyl compounds to produce olefins[10] can be envisioned as proceeding *via* intermediates related to **6**. The dehydration of primary amides to nitriles is a further example of the elimination of lithium oxide to give a multiple bond.[11] We are currently engaged in looking for additional instances of such reactions[12] and in probing the stereochemical details of metal oxide eliminations, which show a strong preference for the formation of *trans* olefins in the epoxide reactions described above.[13]

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[6] T. L. Brown, *Advan. Organometal. Chem.*, **3**, 365 (1965).

[7] For a recent discussion of this point, see G. Köbrich, *Angew. Chem. Intern. Ed. Engl.*, **6**, 41 (1967).

[8] "Handbook of Chemistry and Physics," 46th ed, The Chemical Rubber Co., Cleveland, Ohio, 1965, p D24.

[9] J. A. Marshall, N. H. Andersen, and A. R. Hochstetler, *J. Org. Chem.*, **32**, 113 (1967).

[10] G. Zweifel and R. B. Steele, *Tetrahedron Letters*, 6021 (1966); G. Cainelli, G. D. Bello, and G. Zubiani, *ibid.*, 4315 (1966); G. Cainelli, F. Bertini, P. Grasselli, and G. Zubiani, *ibid.*, 1581 (1967).

[11] E. M. Kaiser and C. R. Hauser, *J. Org. Chem.*, **31**, 3873 (1966); S. E. Ellzey, C. H. Mack, and W. J. Connick, *ibid.*, **32**, 846 (1967); L. G. Humber and M. A. Davis, *Can. J. Chem.*, **44**, 2113 (1966); M. S. Newman and T. Fukunaga, *J. Am. Chem. Soc.*, **82**, 693 (1960).

[12] Unpublished work in these laboratories by Mr. A. C. Clark has shown that *t*-butyllithium and 2-cyclopentenol cleanly produce 3-*t*-butylcyclopentene.

[13] This work was supported by a National Science Foundation research grant (GP-6610).

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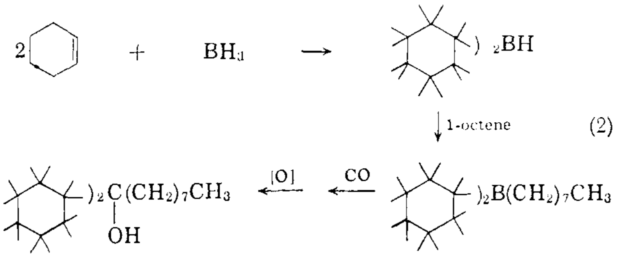
The Carbonylation of Mixed Trialkylboranes. Evidence for the Intramolecular Nature of the Transfer of Groups from Boron to Carbon in the Carbonylation Reaction. A Convenient Synthesis of Unsymmetrical Ketones, RR′CO

Sir:

The reaction of carbon monoxide with trialkylboranes[1] at atmospheric pressure[2] provides a highly convenient synthetic route to tertiary alcohols,[2a] secondary alcohols,[2b] ketones,[2b] and methylol derivatives.[2c] However, these syntheses start with R_3B, with three identical alkyl groups, and lead to tertiary alcohols, to secondary alcohols, and to ketones with identical alkyl groups. The scope of the synthesis would be greatly enhanced by its applicability to the synthesis of derivatives containing different alkyl substituents. We wish to report here the demonstration of the successful synthesis of such derivatives and the extension of this synthesis to products containing a variety of functional groups.[3]

The carbonylation of an equimolar mixture of triethylborane and tri-*n*-butylborane in the presence of ethylene glycol[2a] led to a product, after oxidation, which consisted of a mixture of triethylcarbinol and tri-*n*-butylcarbinol (1). There was no evidence for the presence of any mixed derivatives, such as diethyl-*n*-butylcarbinol or ethyl-di-*n*-butylcarbinol, which would have accompanied an intermolecular transfer of alkyl groups. Similarly, dicyclohexyl-*n*-octylborane, readily synthesized by the reaction of dicyclohexylborane and 1-octene, yielded dicyclohexyl-*n*-octylcarbinol in 82% yield, without evidence of any isomeric materials (2).

$$\mathrm{Et_3B + CO \longrightarrow Et_3CBO \xrightarrow{[O]} Et_3COH}$$
$$n\text{-}\mathrm{Bu_3B + CO} \longrightarrow n\text{-}\mathrm{Bu_3CBO} \longrightarrow n\text{-}\mathrm{Bu_3COH} \qquad (1)$$



(2)

These results, indicating that the groups are transferred intramolecularly from boron to carbon, are consistent with the mechanism previously proposed.[1,2b] They are also promising for extending broadly the utility of this new synthetic route. Hydroboration[4] provides a convenient means for the synthesis of organoboranes containing either two, $R_2R'B$, or three different groups.[5] Consequently, there would appear to be no

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[1] M. E. D. Hillman, *J. Am. Chem. Soc.*, **84**, 4719 (1962); **85**, 982, 1626 (1963).

[2] (a) H. C. Brown and M. W. Rathke, *ibid.*, **89**, 2737 (1967); (b) *ibid.*, **89**, 2738 (1967); (c) M. W. Rathke and H. C. Brown, *ibid.*, **89**, 2740 (1967).

[3] H. C. Brown, G. W. Kabalka, and M. W. Rathke, *ibid.*, **89**, 4530 (1967).

[4] H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

[5] G. Zweifel and H. C. Brown, *J. Am. Chem. Soc.*, **85**, 2066 (1963); G. Zweifel, N. R. Ayyangar, and H. C. Brown, *ibid.*, **85**, 2072 (1963).

Table I. Products from the Carbonylation–Oxidation of Representative Dicyclohexylmonoalkylboranes

Olefin	Unsymmetrical ketone[a]	$n^{20}D$	Yield, %[b]	Ratio, RR'CO:R_2CO
1-Butene	Cyclohexyl *n*-butyl	1.4554	72	3.5
2-Butene	Cyclohexyl *sec*-butyl	1.4535	66	2.7
Isobutene	Cyclohexyl isobutyl	1.4526	36	0.85
1-Octene	Cyclohexyl *n*-octyl	1.4600	71	3.8
Cyclopentene	Cyclohexyl cyclopentyl	1.4825	53	1.2
Norbornene	Cyclohexyl *exo*-norbornyl[c]	1.4992	35	0.68

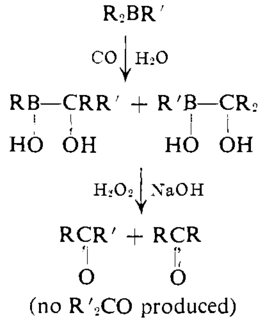
[a] Analytical data within accepted limits were obtained for all new compounds. [b] Yields are based on glpc analysis and are over-all yields based on the amount of olefin taken to react with the dicyclohexylborane. [c] *exo* configuration assigned on the basis of the known *exo* hydroboration of norbornene and the evidence that carbonylation proceeds with retention.[2c]

difficulty in proceeding from such mixed organoboranes to the corresponding mixed tertiary alcohols.

A new problem appears in extending this approach to the synthesis of unsymmetrical ketones. A mixed organoborane, $R_2R'B$, can in theory give rise to two different ketones, the symmetrical product, R_2CO, as well as the desired unsymmetrical ketone, RR'CO. Obviously, if the migratory aptitude of R dominates the reaction, very little of the desired product, RR'CO, would be formed.

In order to learn whether such major variations in the migratory aptitudes of representative groups should be anticipated, we undertook to apply the ketone synthesis to a representative selection of mixed organoboranes, $R_2R'B$. Dicyclohexylborane is readily synthesized by treating cyclohexene with the theoretical quantity of hydroborating agent.[6] This dialkylborane was then treated in individual experiments with 1-butene, 2-butene, isobutene, 1-octene, cyclopentene, and norbornene, to form the corresponding mixed trialkylboranes. These organoboranes, in diglyme solution, were then treated with carbon monoxide at 100° in the presence of added water.[2b] The absorption of carbon monoxide proved to be surprisingly fast, complete reaction requiring less than 1 hr with all of the derivatives examined. Oxidation with alkaline hydrogen peroxide produced a mixture of ketones which were examined by glpc.

In the case of 1-butene there was realized a yield of 72% cyclohexyl *n*-butyl ketone and 20% dicyclohexyl ketone. No di-*n*-butyl ketone was observed, confirming the conclusion that the transfer of alkyl groups is intramolecular in nature (3).



$$\begin{gathered} R_2BR' \\ \mathrm{CO}\Big\downarrow \mathrm{H_2O} \\ R\underset{HO}{B}\!-\!\underset{OH}{C}RR' + R'\underset{HO}{B}\!-\!\underset{OH}{C}R_2 \\ \mathrm{H_2O_2}\Big\downarrow \mathrm{NaOH} \\ R\underset{O}{\underset{\|}{C}}R' + R\underset{O}{\underset{\|}{C}}R \\ \text{(no } R'_2CO \text{ produced)} \end{gathered} \qquad (3)$$

The ratio of cyclohexyl alkyl ketone to dicyclohexyl ketone should be 2 if the transfer of alkyl groups from boron to carbon occurs in a random, statistical manner. Deviations from this ratio reflect the relative migration aptitudes of the cyclohexyl and alkyl groups. The observed ratio varied from 3.8 for dicyclohexyl-*n*-octylborane to 0.68 for dicyclohexyl-*exo*-norbornylborane, as revealed by the summary of the data in Table I. Obviously, the yield of the desired ketone will vary with the relative migratory aptitudes of the groups. However, within the structural variations examined, the migratory aptitudes do not vary sufficiently so as to constitute a serious handicap to the utilization of this procedure for the synthesis of unsymmetrical ketones.

The following procedure for the preparation of cyclohexyl cyclopentyl ketone is representative.

A dry 500-ml flask equipped with thermometer well and magnetic stirring bar was attached to the carbonylation apparatus.[7] The system was flushed with nitrogen and 150 ml of a diglyme solution containing 16.4 g (200 mmoles) of cyclohexene was injected into the reaction flask. The flask was immersed in an ice bath and 51.8 ml (100 mmoles of BH_3) of a solution of diborane in tetrahydrofuran was added dropwise over a period of 10 min. The solution was allowed to come to room temperature and stirred for 1 hr. Cyclopentene, 6.81 g (100 mmoles), was then added and the solution warmed to 45° for 1 hr to complete the hydroboration. The tetrahydrofuran was removed under vacuum[8] and the solution was heated to 100°. Water, 2.7 ml, was then added, the system was flushed with carbon monoxide, and the reaction was initiated by magnetically stirring the contents of the flask vigorously. After 45 min, a total of 100 mmoles of carbon monoxide had been absorbed. The flask was cooled in an ice–water bath and oxidation accomplished by adding 33 ml of 3 *M* sodium hydroxide, followed by the dropwise addition of 23 ml of 30% hydrogen peroxide at a rate sufficient to maintain the temperature at 35°. The solution was stirred for 1 hr at 30–35° to ensure completion of the oxidation. The aqueous phase was saturated with sodium chloride, and the organic phase, dried over magnesium sulfate, was analyzed by glpc. The analysis revealed the presence of 53 mmoles of cyclohexyl cyclopentyl ketone, a yield of 53%, and 43 mmoles of dicyclohexyl ketone.

It is apparent that the optimum applicability of this method will depend on the development of simple synthetic routes to both monoalkylboranes and dialkyl-

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(6) H. C. Brown and A. W. Moerikofer, *J. Am. Chem. Soc.*, **84**, 1478 (1962).

(7) We used a commercial model of the Brown hydrogenator (available from the Delmar Scientific Laboratories, Maywood, Ill. 60154) adapted for the automatic generation of carbon monoxide, as described by M. W. Rathke and H. C. Brown, *J. Am. Chem. Soc.*, **88**, 2606 (1966).

(8) As reported in the following communication,[3] the carbonylation in many cases proceeds quite satisfactorily at 45°, so that removal of the tetrahydrofuran may not be necessary. Indeed, as described there, the entire procedure may be carried out in tetrahydrofuran solution, providing a more convenient over-all procedure.

boranes[9] and a more detailed knowledge of the influence of structure on the migratory aptitude of various groups. However, even in the present state of our knowledge, it is evident that we have a new, highly convenient synthetic route to a wide variety of mixed tertiary alcohols, secondary alcohols, and ketones.

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[9] For example, the commercial availability of dimethylborane and diethylborane in a conveniently handled form would make the methyl and ethyl ketones readily available from any derivative which can be hydroborated to form the mixed organoborane.

[10] National Science Foundation Fellow, 1964–1966.

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The Carbonylation of Mixed Trialkylboranes Containing Substituents as a Synthetic Route to Unsymmetrical Ketones with Such Functional Substituents. A New Simple Route for the Conversion of Olefins, $RCH{=}CH_2$, into the Corresponding Carboxylic Acids, $RCH_2CH_2CO_2H$

Sir:

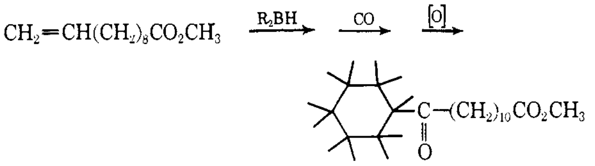
The hydroboration reaction can tolerate the great majority of functional groups. We wish to report that the carbonylation of organoboranes[2,3] is likewise tolerant of functional groups. Hydroboration–carbonylation–oxidation provides a synthetic route to tertiary alcohols, secondary alcohols, ketones, and methylol derivatives, compounds characteristic of many types of syntheses involving the reactive Grignard reagent. However, whereas the use of the Grignard reagent is necessarily restricted to the use of building blocks which do not contain reactive substituents, the present synthetic approach is evidently capable of utilizing building blocks containing a wide variety of reactive functional groups.

To explore the synthetic possibilities of this new development we decided to utilize dicyclohexylborane as a reagent to react with a number of olefins containing a variety of representative functional groups. Carbonylation of the resulting organoborane in the presence of water should yield a functionally substituted cyclohexyl monoalkyl ketone,[4] provided that the substituent does not interfere with the desired reaction.

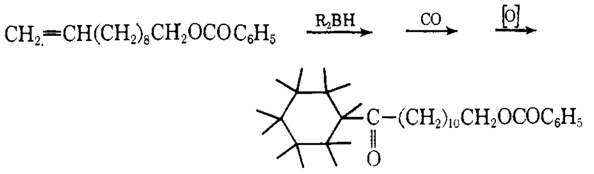
Previously, we had carried out the carbonylation at 100°.[4] The high temperature made it necessary to utilize a solvent of relatively low volatility, such as diglyme. However, the remarkable reactivity of the dicyclohexylmonoalkylboranes encouraged us to explore the use of lower temperatures (45°), permitting the use of the more convenient solvent, tetrahydrofuran. As an additional bonus, we discovered that the lower reaction temperature results in a considerably more selective migration of the alkyl group. Thus, carbonylation of dicyclohexyl-*n*-octylborane at 100°, followed by oxidation, produces a 90% yield of ketones, composed of 79% cyclohexyl *n*-octyl ketone and 21% dicyclohexyl ketone. When the same reaction is carried out in tetrahydrofuran at 45°, the total yield of ketone was 86%, composed of 92% cyclohexyl *n*-octyl ketone and only 8% dicyclohexyl ketone.

We applied this reaction to methyl 10-undecenoate, 10-undecenyl benzoate, allyl benzoate, ethyl vinylacetate, and allyl cyanide. We encountered difficulties in attempting to put some of these polyfunctional derivatives through the gas chromatograph. Consequently, we finally decided to rely on the isolation of either crystallized or distilled products.

The functional groups tested offered no evident difficulty. Thus methyl 10-undecenoate was converted into methyl 12-cyclohexyl-12-oxododecanoate, mp 37.5–38.0°, in 53% isolated yield (1). Similarly, 10-undecenyl benzoate was converted into the corresponding cyclohexyl ketone, mp 43.5–44°, in 61% yield (2).

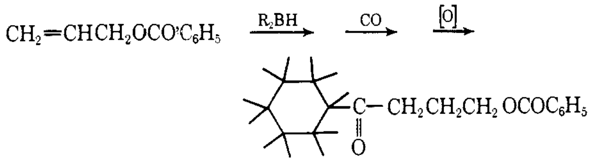


(1)

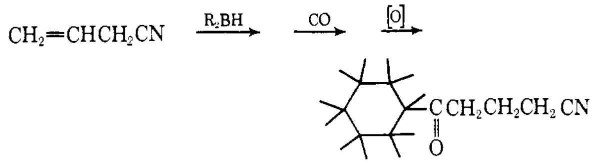


(2)

It is extremely promising that even in cases where the functional group is quite close to the double bond, as in allyl benzoate (3) and allyl cyanide (4), the reaction apparently proceeds without significant complications.



(3)



(4)

The experimental results are summarized in Table I.

The following procedure for the conversion of 10-undecenyl benzoate into 12-cyclohexyl-12-oxododecyl benzoate is representative. A dry 300-ml flask equipped with a thermometer well and magnetic stirring bar was attached to the carbonylation apparatus,[4] and the system was flushed with nitrogen. A solution of 8.2 g (100 mmoles) of cyclohexene in 22 ml of tetrahydrofuran was introduced and the flask was immersed in an ice-water bath. Hydroboration was achieved by the dropwise addition of 28 ml of a solution of diborane (50 mmoles of BH_3) in tetrahydrofuran. The solution was stirred at room temperature and 13.4 g of 10-un-

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[1] H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

[2] M. E. D. Hillman, *J. Am. Chem. Soc.*, **84**, 4715 (1962); **85**, 982, 1636 (1963).

[3] H. C. Brown and M. W. Rathke, *ibid.*, **89**, 2737 (1967); **89**, 2738 (1967); M. W. Rathke and H. C. Brown, *ibid.*, **89**, 2740 (1967).

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