Interestingly, the reaction opens a pathway for the biological oxidative decarboxylation of α-ketoglutarate other than that catalyzed by α-ketoglutarate dehydrogenase (EC 1.2.4.2) which requires thiamine pyrophosphate, lipoate, and FAD as cofactors.

hydroxyphenylpyruvate hydroxylase (EC 1.14.2.2) in an $^{18}O_2$-enriched atmosphere. Two atoms of molecular oxygen were incorporated into the formed homogentisic acid. Thus, in this case an intramolecular reaction of the same type as the one discussed in this communication had occurred, and *p*-hydroxyphenylpyruvate hydroxylase belongs to the class of oxygenases utilizing α-keto acid as reductant.

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Reaction of B-Alkyl-9-borabicyclo[3.3.1]nonanes with Carbon Monoxide in the Presence of Lithium Tri-*t*-butoxyaluminohydride. The Conversion of Functionally Substituted Olefins into Aldehydes *via* Hydroboration

Sir:

We wish to report that the B-alkyl-9-borabicyclo[3.3.1]nonanes[1] (B-R-9-BBN) react readily with carbon monoxide in the presence of lithium tri-*t*-butoxyaluminohydride,[2,3] without reduction of functional substituents. This development makes possible the facile introduction of the aldehyde group into olefins containing many representative functional substituents (eq 1–5).

$$\mathrm{H_2C{=}CH(CH_2)_8CO_2CH_3 \longrightarrow \underset{99\%}{OHC(CH_2)_{10}CO_2CH_3}} \qquad (1)$$

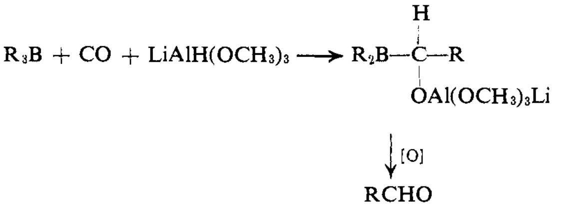
$$\mathrm{H_2C{=}CH(CH_2)_8CN \longrightarrow \underset{95\%}{OHC(CH_2)_{10}CN}} \qquad (2)$$

$$\mathrm{H_2C{=}CHCH_2CO_2C_2H_5 \longrightarrow \underset{83\%}{OHC(CH_2)_3CO_2C_2H_5}} \qquad (3)$$

$$\mathrm{H_2C{=}CHCH_2CN \longrightarrow \underset{85\%}{OHCCH_2CH_2CH_2CN}} \qquad (4)$$

$$\mathrm{H_2C{=}CHCH_2O_2CC_6H_5 \longrightarrow \underset{89\%}{OHCCH_2CH_2CH_2O_2CC_6H_5}} \qquad (5)$$

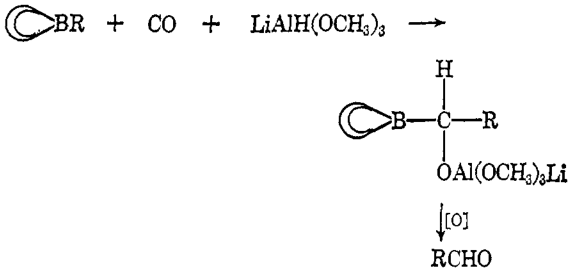
We recently reported that carbon monoxide reacts rapidly and essentially quantitatively with trialkylboranes in the presence of lithium trimethoxyaluminohydride, providing a highly useful synthetic route to the corresponding homologated aldehydes[4] (eq 6). Unfortunately, in this synthesis only one of the three alkyl groups in the organoborane is utilized for the production of aldehyde.



$$\mathrm{R_3B + CO + LiAlH(OCH_3)_3 \longrightarrow R_2B{-}\overset{H}{\underset{OAl(OCH_3)_3Li}{C}}{-}R \xrightarrow{[O]} RCHO} \qquad (6)$$

More recently we noted that the application of the B-alkyl-9-borabicyclo[3.3.1]nonanes (eq 7) overcame this difficulty[5] (eq 8). This development provided an exceptionally simple procedure for introducing an aldehyde group into alkenes and dienes of a wide variety of structures in highly satisfactory yields.[5]

(7)



(8)

Hydroboration is a mild reaction which can tolerate many functional groups.[6] Consequently, there is no problem in preparing the B-R-9-BBN derivatives containing functional substituents in the B-R group. On the other hand, lithium trimethoxyaluminohydride is a powerful reducing agent,[7] approaching lithium aluminum hydride in effectiveness. It was therefore quite clear that the usual procedure of introducing carbon monoxide into a mixture of the organoborane and metal hydride would be unsatisfactory.

Fortunately, it was observed that the slow addition of a solution of lithium trimethoxyaluminohydride in THF to a well-stirred THF solution of B-R-9-BBN, saturated with carbon monoxide,[8] gave reasonable yields of the desired aldehydes containing reducible functional substituents. Evidently the reagent reacts much more rapidly with the carbonyl intermediate than

Table I. A Comparison of Lithium Trimethoxyaluminohydride and Lithium Tri-*t*-butoxyaluminohydride for the Carbonylation of Functionally Substituted B-Alkyl-9-borabicyclo[3.3.1]nonane Derivatives[a]

		Yield, %[b]	
Olefin	Product	LiAlH-(OCH$_3$)$_3$	LiAlH-(O-*t*-Bu)$_3$
Methyl 10-undecenoate	11-Carbomethoxy undecanol	99	99
3-Buten-1-yl acetate	5-Acetoxypentanal	45	92
Allyl benzoate	4-Benzoxybutanal	25	89

[a] All reactions were carried out at −25°, utilizing equimolar amounts of the B-R-9-BBN and the metal hydride. [b] Yields by glpc analysis.

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(1) E. F. Knights and H. C. Brown, *J. Am. Chem. Soc.*, **90**, 5280, 5281, 5283 (1968).

(2) H. C. Brown and R. F. McFarlin, *ibid.*, 80, 5372 (1958).

(3) The reagent is available from the Ventron Corp., Beverly Mass. 01915.

(4) H. C. Brown, R. A. Coleman, and M. W. Rathke, *J. Am. Chem. Soc.*, **90**, 499 (1968).

(5) H. C. Brown, E. F. Knights, and R. A. Coleman, *ibid.*, **91**, 2144 (1969).

(6) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

(7) H. C. Brown and P. M. Weissman, *ibid.*, 87, 5614 (1965).

(8) We used a commercial model of the automatic hydrogenator (Delmar Scientific Laboratories, Maywood, Ill. 60154), adapted for carbonylations as previously described: M. W. Rathke and H. C. Brown, *ibid.*, 88, 2606 (1966).

Table II. Conversion of Functionally Substituted Olefins into Aldehydes *via* Hydroboration with 9-BBN and Carbonylation in the Presence of Lithium Tri-*t*-butoxyaluminohydride[a]

Olefin	Product[b]	Yield, % Glpc	Yield, % Isolated	Properties n^{20}D	Properties Bp, °C (mm)	Properties 2,4-DNP mp, °C
Methyl 10-undecenoate	10-Carbomethoxy-undecanal	99	85	1.4452	115–118 (1.5)	70–71.5
10-Undecenenitrile	10-Cyanododecanal	99	83	1.4542	120–122 (1.2)	60–62
10-Undecen-1-yl acetate	12-Acetoxy-dodecanal	99	87	1.4460	110–112 (0.3)	75–77
Allyl benzoate	4-Benzoxybutanal	89	74	1.5243	116–118 (0.5)	76.5–77.5[c]
Ethyl vinylacetate	4-Carbethoxy-butanal	83	70	1.4259	68 (1.5)	69–70[d]
Allyl cyanide	4-Cyanobutanal	85	72	1.4262	83.5 (2)	117–118[e]
3-Buten-1-yl acetate	5-Acetoxypentanal	92	84	1.4284	66–67 1.5)	99–100[f]

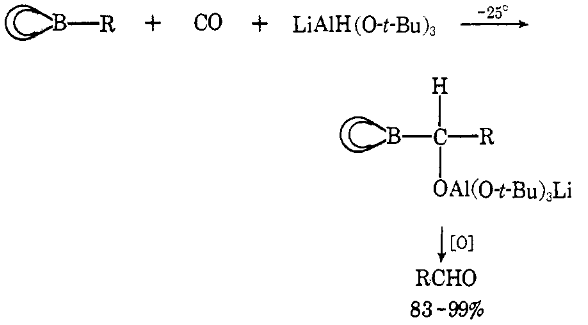
[a] Procedure followed that described for methyl 10-undecenoate. [b] All spectroscopic data and elemental analyses were in agreement with the structure indicated. [c] Lit. mp 77.5°. [d] Lit. mp 70–70.5°. [e] Lit. mp 117–118°. [f] Lit. mp 100°.

with the reducible groups. Representative results are summarized in Table I.

The yields, while quite satisfactory for the longer chain derivative, dropped off seriously for the shorter chain derivatives. Evidently, in these derivatives reduction of the functional groups competes seriously with reduction of the carbonyl intermediate.

It appeared that this difficulty might be solved by use of a milder reducing agent. Lithium tri-*t*-butoxyaluminohydride is such a mild reducing agent.[9] Indeed, under standard conditions (0°, THF) it does not reduce esters or nitriles.[9] Fortunately, it reduces nicely the postulated carbonyl intermediate from B-R-9BBN, even though it had previously failed to react with the intermediate from the usual trialkylborane.[10] Evidently this is another indication of the much less hindered environment at the bridgehead position of B-R-9-BBN[11] and its carbonyl derivative.[1]

In any event, the use of lithium tri-*t*-butoxyaluminohydride solved the difficulties previously encountered and gave excellent yields for both short- and long-chain derivatives (eq 9). Representative results are summarized in Table II.



(9)

The following procedure describing the conversion of methyl 10-undecenoate into 11-carbomethoxyundecanal is representative. The dried reaction vessel of the automatic carbonylator[8] was flushed with nitrogen and charged with 20 ml of THF and 9.9 g (50 mmoles) of methyl 10-undecenoate. Hydroboration was achieved by adding slowly (over 20 min) 100 ml of a 0.5 *M* solution of 9-BBN in THF. After 15 min, reaction was initiated by flushing the system with carbon monoxide from the generator, cooling the flask to approximately −25 to −35°,[12] and adding 50 ml of a 1.0 *M* solution of lithium tri-*t*-butoxyaluminohydride over 45 min. Complete absorption of carbon monoxide required an additional 90 min. The reaction mixture was brought to room temperature, 120 ml of a buffer of pH 7 was added (a water solution 2.2 *M* in NaH_2PO_4 and K_2HPO_4), and oxidation was carried out by the dropwise addition of 21 ml of 30% hydrogen peroxide, keeping the temperature below 30°. The THF phase was twice washed with a saturated sodium chloride–water solution and then stirred for 1 hr with 100 ml of a saturated aqueous sodium bisulfite solution. The precipitated adduct was washed and then treated with 50 ml of a saturated aqueous magnesium sulfate solution, 50 ml of pentane, and 5 ml of a 40% solution of formaldehyde.[13] After the bisulfite adduct had disappeared (30 min), the pentane layer was removed. Distillation yielded 9.7 g (85%) of 11-carbomethoxyundecanal, bp 115–118° (1 mm), n^{20}D 1.4452, 2,4-DNP mp 70–71.5°.

This study emphasized nitrile and ester derivatives as containing relatively easily reducible groups and thereby provided a severe test. There would appear to be no difficulty in extending the procedure to structures containing less readily reducible groups, such as halo, nitro, or sulfone.[14] Consequently, this aldehyde synthesis appears to be both simple and of very wide generality and should find an important place in synthetic work.

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[9] H. C. Brown and P. M. Weissman, *Israel J. Chem.*, 1, 430 (1963).

[10] Unpublished research of R. A. Coleman.

[11] H. C. Brown, M. M. Rogić, H. Nambu, and M. W. Rathke, *J. Am. Chem. Soc.*, **91**, 2147 (1969).

[12] The carbonylation reaction had previously been carried out at 0°.[6] However, we have since observed that at −25 to −35° the B-alkyl group of B-R-9-BBN migrates almost exclusively, to the practical exclusion of a cyclooctylboron migration, providing almost quantitative yields of the desired derivatives.

[13] This procedure for the regeneration of aldehyde from the bisulfite adduct proved to be the best of those examined. It is described by J. W. Cornforth, "Organic Syntheses," Coll. Vol. IV, John Wiley & Sons, Inc., New York, N. Y., 1963, p 757.

[14] We have successfully converted *m*-nitrostyrene into *m*-nitrohydrocinnamaldehyde.

[15] Recipient of a National Science Foundation Traineeship at Purdue University.