ate to 1,3-dimethyl-6-hydrazinouracil has been shown to give 1,3-dimethyl-5-(1,2-dicarbethoxyhydrazino)-6-hydrazinouracil.[8] Cyclization of this compound with sodium ethoxide in absolute ethanol gave the sodium salt of 6,8-dimethylpyrimido[5,4-*e*]-*as*-triazine-3,5,7(2H,-6H,8H)-trione[8] (**4**) (fervenulone), which was filtered, suspended in fresh absolute ethanol, and treated with methyl iodide. Stirring for 2 hr at 50° then gave 2-methylfervenulone (**1**) in 60% yield. Alternatively, **4** was prepared by treatment of **2** with hydrazine in chloroform solution to give 4-(6-chloro-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)semicarbazide (**5**), mp 178–179° (33%). Pyrolysis of **5** at 135–140° (0.01 mm) afforded 1,4-dihydro-6,8-dimethylpyrimido[5,4-*e*]-*as*-triazine-3,5,7(2H,6H,8H)-trione (**6**), mp 250–251° (27%), which was oxidized to **4** in 88% yield by stirring with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in refluxing chloroform solution.

In the course of the above work an interesting rearrangement was observed upon pyrolytic cyclization of **3**. Heating **3** at 135° (0.01 mm) for 6 hr gave 1,4-dihydro-1,6,8-trimethylpyrimido[5,4-*e*]-*as*-triazine-3,5,7-(2H,6H,8H)-trione (**7**), mp 241–242° dec (66%). This compound is isomeric with dihydro-**1** but is incapable of dehydrogenation and thus provides independent evidence for the absence of a methyl group on N-1 in MSD-92. An independent, unequivocal synthesis of **7** was achieved by heating **2** in methanol solution to give the urethan **8**, mp 169–170° (80%), which upon treatment with methylhydrazine for 2 hr in acetonitrile solution at room temperature gave 1,3-dimethyl-5-carbomethoxyamino-6-(1-methylhydrazino)uracil (**9**), mp 179–180° dec (46%) (benzylidene derivative, mp 159–160°). Cyclization of **9** by heating in ethanol with sodium ethoxide then gave **7** in 38% yield.

2-Methylfervenulone (MSD-92) (**1**) is one of the three possible methyl derivatives of fervenulone (**4**). We also report at this time the synthesis of both remaining methyl isomers. 3-Methoxy-6,8-dimethylpyrimido[5,4-*e*]-*as*-triazine-5,7(6H,8H)-dione (**11**), mp 144–145° (85%), was formed by treating 3-chloro-6,8-dimethylpyrimido[5,4-*e*]-*as*-triazine-5,7(6H,8H)-dione[8] (**10**) with sodium methoxide for 15 min at room temperature. Finally, treating a solution of **4** in methanol with diazomethane gave the only remaining methyl isomer, 4,6,8-trimethylpyrimido-[5,4-*e*]-*as*-triazine-3,5,7-(4H,6H,8H)-trione (**12**), mp 218–220° dec (5%), along with smaller amounts of both **1** and **11**.

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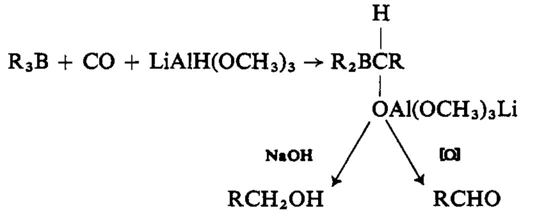
Received January 3, 1969

Reaction of B-Alkyl-9-borabicyclo[3.3.1]nonanes with Carbon Monoxide in the Presence of Lithium Trimethoxyaluminohydride. A Convenient Procedure for the Conversion of Olefins into Aldehydes *via* Hydroboration

Sir:

We previously 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 aldehyde or methylol derivative[1] (1).

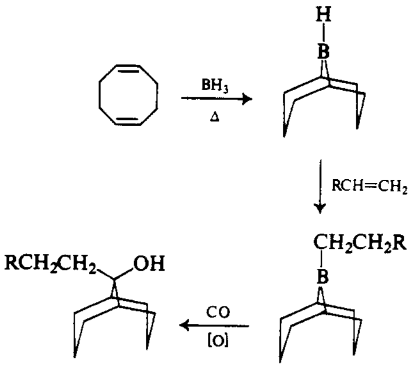


$$R_3B + CO + LiAlH(OCH_3)_3 \rightarrow R_2\overset{H}{\underset{OAl(OCH_3)_3Li}{BCR}} \quad (1)$$

$$\xrightarrow{NaOH} RCH_2OH \qquad \xrightarrow{[O]} RCHO$$

Based on the equation as written, the yields were essentially quantitative. However, since only one of the three groups on boron participates in the desired reaction, the conversion of alkyl groups to the desired product is a maximum of 33%. This represents a considerable difficulty for many of the new reactions of organoboranes[2] in cases where a valuable intermediate is to be converted into the desired product.

1,5-Cyclooctadiene undergoes cyclic hydroboration with remarkable ease.[3a] The resulting bibyclic borane, 9-borabicyclo[3.3.1]nonane (9-BBN), exhibits unusual stability in air, but is a very active hydroborating agent, converting olefins into the corresponding B-alkyl derivatives.[3b] Carbonylation readily converts these B-alkyl derivatives into the corresponding tertiary alcohols[3c] (2).



(2)

We now wish to report that the use of 9-BBN solves the above problem for the new aldehyde synthesis. B-Alkyl-9-borabicyclo[3.3.1]nonanes react rapidly at 0° with carbon monoxide in the presence of lithium trimethoxyaluminohydride. The resulting intermediate can be hydrolyzed to the methylol derivative or oxidized to the aldehyde. High yields are realized, indicating that the B-alkyl group migrates in preference to the ring-boron bonds (3). (It is convenient to use the symbol shown in eq 3 for 9-BBN.)

The usual range of olefin structures can evidently be accommodated, as indicated by the following examples (4–6).

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

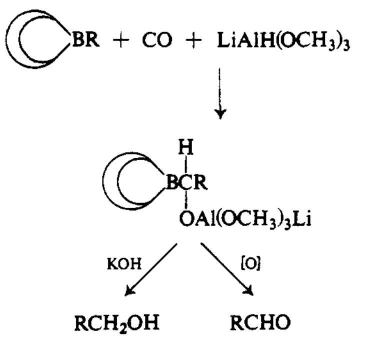
(2) J. J. Tufariello, L. T. C. Lee, and P. Wojkowski, *ibid.*, **89**, 6804 (1967); A. Suzuki, A. Arase, H. Matsumoto, M. Itoh, H. C. Brown, M. M. Rogić, and M. W. Rathke, *ibid.*, **89**, 5708 (1967); H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **89**, 5709 (1967); H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **90**, 818, 1911 (1968); H. C. Brown, M. M. Rogić, and M. W. Rathke, *ibid.*, **90**, 6218 (1968); J. Hooz and S. Linke, *ibid.*, **90**, 5936, 6891 (1968).

(3) (a) E. F. Knights and H. C. Brown, *ibid.*, **90**, 5280 (1968); (b) *ibid.*, **90**, 5281 (1968); (c) *ibid.*, **90**, 5283 (1968).

Table I. Aldehydes Produced *via* the Hydroboration–Carbonylation of Representative Olefins Using 9-BBN

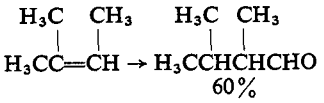
Olefin	Aldehyde	Yield, %[a] 25°	Yield, %[a] 0°
1-Hexene	*n*-Heptaldehyde	77[b]	93
Isobutylene	Isovaleraldehyde	52	
2-Methyl-2-butene	2,3-Dimethylbutanal	54	60
2,3-Dimethyl-2-butene	No reaction		
Cyclopentene	Cyclopentanecarboxaldehyde	79[b]	
Cyclohexene	Cyclohexanecarboxaldehyde	77[b]	81
Styrene	Hydrocinnamaldehyde	84	
Norbornene	Norbornane-2-carboxaldehyde[c]	59	
1,5-Hexadiene	Suberaldehyde[d]	60	78
4-Vinylcyclohexene	3-(3-Cyclohexenyl)propanal		93

[a] Yields were established by glpc analysis of the alcohols produced by reduction of the aldehydes with sodium borohydride. An internal standard of *p*-dimethoxybenzene was used, and peak positions and response ratios were established with authentic samples available from other studies. [b] Treatment of the product with ethanolic potassium hydroxide produced almost identical yields of the corresponding methylol derivative. [c] We believe this is the *exo* isomer, from the stereospecificity of the hydroboration stage. However, we did not attempt to establish the isomer distribution. [d] Identified as the diol, mp 61–62° (lit. mp 63°); diphenylurethan mp 171–172° (lit. mp 172–172.5°).

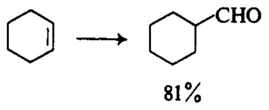


(3)

$$CH_3(CH_2)_3CH{=}CH_2 \rightarrow \underset{93\%}{CH_3(CH_2)_5CHO} \quad (4)$$

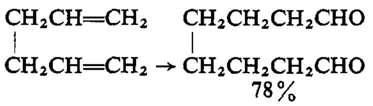


$$H_3C\overset{\substack{H_3C\\|}}{C}{=}\overset{\substack{CH_3\\|}}{C}H \rightarrow \underset{60\%}{H_3C\overset{\substack{H_3C\\|}}{C}H\overset{\substack{CH_3\\|}}{C}HCHO} \quad (5)$$



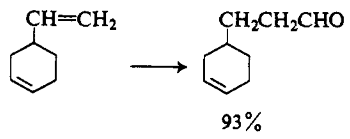
(6)

Dienes are readily accommodated to produce the corresponding diols or dialdehydes (7).



$$\begin{array}{l}CH_2CH{=}CH_2\\ |\\ CH_2CH{=}CH_2\end{array} \rightarrow \underset{78\%}{\begin{array}{l}CH_2CH_2CH_2CHO\\ |\\ CH_2CH_2CH_2CHO\end{array}} \quad (7)$$

Finally, it is possible to utilize the selective characteristics of hydroboration with 9-BBN to achieve the selective conversion of a diene into the unsaturated aldehyde (8).



(8)

We are currently exploring the possibility of extending this synthesis to unsaturated compounds containing a wide variety of functional substituents.[4]

Representative results are summarized in Table I.

The following procedure involving the conversion of 4-vinylcyclohexene into 3-(3-cyclohexenyl)propanol (8) is representative.

A dry flask, equipped with a septum inlet, thermometer well, magnetic stirrer, and reflux condenser, was flushed with nitrogen and then maintained under a static pressure of the gas. The flask was charged with 30 ml of tetrahydrofuran and 2.16 g (20 mmol) of 4-vinylcyclohexene and immersed in an ice bath. Selective hydroboration of the vinylic group was achieved by adding 35 ml of a 0.60 *M* solution of 9-BBN (21 mmol) in THF to the cold, well-stirred solution of the diene. In the reaction flask of the carbonylation apparatus there was generated 21 mmol of lithium trimethoxyaluminohydride from the addition of 15.75 ml of a 4.0 *M* solution of methanol in THF to 14.0 ml of a 1.50 *M* solution of lithium aluminum hydride in THF. The above solution of B-R-9-BBN was introduced with the aid of a syringe, the system flushed with carbon monoxide (from the automatic carbonylator[5]), and carbonylation initiated by starting the magnetic stirrer. Carbon monoxide uptake was rapid, with 21 mmol being absorbed in 15 min. The system was then flushed with nitrogen, 40 ml of a pH 7 buffer was added (a water solution 2.5 *M* in NaH_2PO_4 and in K_2HPO_4), and oxidation carried out by the dropwise addition of 7.0 ml of 30% hydrogen peroxide, keeping the temperature below 20°. The mixture was then extracted with 100 ml of pentane and the pentane phase twice washed with 50-ml portions of water. The solvents were removed on a rotary evaporator and the aldehyde was recovered on an F & M 776 preparative gas chromatograph. Glpc analysis indicated a 93% yield. There was isolated 2.41 g (83%) of 3-(3-cyclohexenyl)propanal, bp 202.5° (745 mm), $n^{20}\text{D}$ 1.4738, 2,4-DNP mp 106–106.5°.

In summary, these results reveal that a large variety of olefinic structures are readily converted to aldehydes or methylol derivatives in good yield *via* their 9-BBN derivatives. This surmounts the difficulty previously

(4) Research in progress with Randolph A. Coleman.

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

encountered in many reactions of organoboranes in which only one of the three groups on boron is utilized.[2] Indeed, we have observed that the B-R-9-BBN derivatives may be advantageously utilized in the alkylation of esters,[6] the alkylation of ketones,[7] and the synthesis of cyclopropanes.[8]

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Received December 23, 1968

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[6] H. C. Brown and M. M. Rogic, *J. Am. Chem. Soc.*, **91**, 2146 (1969).

[7] H. C. Brown, M. M. Rogic, H. Nambu, and M. W. Rathke, *ibid.*, **91**, 2147 (1969).

[8] H. C. Brown and S. P. Rhodes, *ibid.*, **91**, 2149 (1969).

[9] Graduate research assistant on Grant GM 10937 from the National Institutes of Health.

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

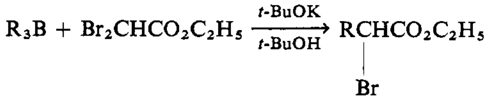
Reaction of B-Alkyl-9-borabicyclo[3.3.1]nonanes with Ethyl Mono- and Dihaloacetates under the Influence of Potassium *t*-Butoxide. A Convenient Procedure for the Conversion of Olefins into Esters or α-Halo Esters *via* Hydroboration

Sir:

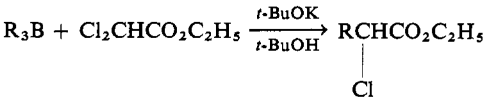
We recently reported that trialkylboranes undergo facile reaction with ethyl bromoacetate under the influence of potassium *t*-butoxide,[1] providing a remarkably simple synthesis of esters with the addition of a two-carbon moiety to the structure (carbethoxymethylation) (1). This reaction can be extended to ethyl di-

$$R_3B + BrCH_2CO_2C_2H_5 \xrightarrow[t\text{-BuOH}]{t\text{-BuOK}} RCH_2CO_2C_2H_5 \qquad (1)$$

bromoacetate or ethyl dichloroacetate, providing an equally simple synthesis of the corresponding α-halocarboxylic acid esters[2] (2, 3).



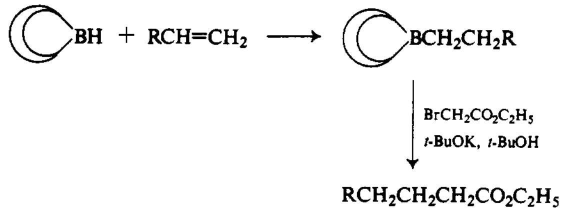
$$R_3B + Br_2CHCO_2C_2H_5 \xrightarrow[t\text{-BuOH}]{t\text{-BuOK}} \underset{\displaystyle Br}{RCHCO_2C_2H_5} \qquad (2)$$



$$R_3B + Cl_2CHCO_2C_2H_5 \xrightarrow[t\text{-BuOH}]{t\text{-BuOK}} \underset{\displaystyle Cl}{RCHCO_2C_2H_5} \qquad (3)$$

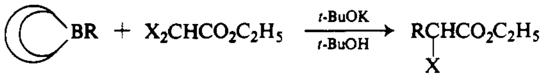
Unfortunately, in these carbethoxymethylation reactions, as in the related one-carbon-atom homologation (carbonylation)[3] and three-carbon-atom homologation (γ-propanalation)[4] reactions, only 33% of the olefin used to form the organoborane, or one of the three alkyl groups on the organoborane, R_3B, is utilized. This limitation could constitute a major difficulty in cases where it is desired to apply these homologation reactions to valuable intermediates.

We previously reported that the use of the B-alkyl-9-borabicyclo[3.3.1]nonanes (B-R-9-BBN)[5] solved this difficulty for the aldehyde synthesis.[6] We now wish to report that the use of these intermediates likewise solves this difficulty for the ester synthesis (4).



(4)

The yields observed were in the range of 50–80%, indicating some competition between migration of the B-alkyl group and the boron–cyclooctyl bond. However, preferential migration of the B-alkyl groups was greatly enhanced in the corresponding reactions with ethyl dibromoacetate and ethyl dichloroacetate, providing the corresponding α-halocarboxylic acid esters in yields of 70–90% (5).



(5)

The results are summarized in Table I.

The following procedure is illustrative. A dry flask equipped with the usual accessories[6] and maintained under nitrogen was charged with 170 ml of tetrahydrofuran and 28.6 ml of a solution of borane (100 mmol) in the same solvent. To the stirred solution at room temperature 12.3 ml (100 mmol) of *cis*-1,5-cyclooctadiene was added over a period of 15 min. At the end of the addition, the temperature had risen to 55–60°. The reaction mixture was refluxed for 1.5 hr and then cooled to 45°. Cyclohexene, 10.1 ml (100 mmol), was introduced and the reaction mixture stirred at 45–50° for 2 hr and then cooled in an ice bath. (The hydroboration of cyclohexene is relatively slow). In most other cases the hydroboration with 9-BBN[5] is complete in a few minutes at 25°.) *t*-Butyl alcohol, 50 ml, and 12.2 ml (100 mmol) of ethyl dichloroacetate was introduced followed by the dropwise addition of 100 ml of 1.00 *M* potassium *t*-butoxide in *t*-butyl alcohol over a period of 30 min. Glpc analysis of the reaction mixture indicated an 81% yield of ethyl α-chlorocyclohexylacetate. To the reaction mixture was added 33 ml of 3 *M* sodium acetate, followed by dropwise addition of 22 ml of 30% of hydrogen peroxide. The reaction mixture was stirred at room temperature for 30 min and then saturated with sodium chloride. The organic layer was separated, dried over magnesium sulfate, and distilled. There was obtained

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[1] H. C. Brown, M. M. Rogic, M. W. Rathke, and G. W. Kabalka, *J. Am. Chem. Soc.*, **90**, 818 (1968).

[2] H. C. Brown, M. M. Rogic, M. W. Rathke, and G. W. Kabalka, *ibid.*, **90**, 1811 (1968).

[3] H. C. Brown, R. A. Coleman, and M. W. Rathke, *ibid.*, **90**, 499 (1968).

[4] H. C. Brown, M. M. Rogic, M. W. Rathke, and G. W. Kabalka, **89**, 5709 (1967); H. C. Brown, G. W. Kabalka, M. W. Rathke, and M. M. Rogić, *ibid.*, **90**, 4165 (1968); H. C. Brown, M. W. Rathke, G. W. Kabalka, and M. M. Rogić, *ibid.*, **90**, 4166 (1968).

[5] E. F. Knights and H. C. Brown, *ibid.*, **90**, 5280, 5281, 5283 (1968).

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