Table I. Reduction of Representative Cyclic and Bicyclic Ketones by Lithium Perhydro-9b-borophenalylhydride[a]

Ketone	Alcohol epimer	Epimer, % LiAlH$_4$[b]	 LiAlH-(OMe)$_3$[b]	 IPC$_2$BH[c]	 LiBH-(*n*-Bu)$_3$	 3
2-Methylcyclopentanone	*cis*	24	44	94	67	94
2-Methylcyclohexanone	*cis*	24	69	94	85	97
3-Methylcyclohexanone	*trans*	16[d]		35		59
3-*t*-Butylcyclohexanone	*trans*	15[d]		28		72
4-Methylcyclohexanone	*cis*	17[d]		33		52
4-*t*-Butylcyclohexanone	*cis*	8[e]		37		54
3,3,5-Trimethylcyclohexanone	*trans*	82[e]				99
Norcamphor	*endo*	89	98	94	98	99
Camphor	*exo*	92	99	100	98	99

[a] In THF at 0°. [b] H. C. Brown and H. R. Deck, *J. Amer. Chem. Soc.*, **87**, 5620 (1965). [c] V. K. Varma, Ph.D. Thesis, Purdue University, Lafayette, Ind., 1967. [d] Present work. [e] P. T. Lansbury and R. E. MacLeay, *J. Org. Chem.*, **28**, 1940 (1963).

none gave 94% of *cis*-2-methylcyclopentanol and 2-methylcyclohexanone gave the corresponding *cis* alcohol in 97% epimeric purity. Norcamphor gave 99% pure *endo*-norborneol, whereas camphor gave the *exo* isomer in 99% epimeric purity. 3,5,5-Trimethylcyclohexanone gives the *trans* isomer almost exclusively (99%). Even in the case of simple cyclohexanones containing a single alkyl substituent in the 3 or the 4 position there is observed a significant shift from the usual predominant attack of the reagent from the axial direction toward attack from the equatorial direction. Indeed 3-*t*-butylcyclohexanone gives 72% of the *trans* isomer as compared to only 15% with lithium aluminum hydride. These results are summarized in Table I.

Previously we had observed that steric control of the reduction of such ketones could be achieved by the use of dialkylboranes, in which the alkyl groups were quite bulky, as in disiamylborane and diisopinocampheylborane (IPC$_2$BH).[6,7] A disadvantage of this approach was the slowness of the reaction using the more hindered dialkylboranes. Thus, the reduction of camphor by diisopinocampheylborane is very slow and requires 24 hr to approach completion.[7] This difficulty is overcome with the present reagent **3**. In all cases, even in the reduction of the highly hindered camphor structure, the reaction is 100% complete within 0.5 hr at 0°.

A further advantage of the reagent is the fact that it contains only one active hydride. This should facilitate kinetic examination of the rates of reaction from the axial and equatorial directions and thereby facilitate resolution of the problem of the factors controlling the formation of epimeric ketones.[8]

Solutions of the trialkylborohydrides were prepared by refluxing for 3 hr in THF 1 equiv of the trialkylborane with an excess of finely divided lithium hydride (usually in moderate excess). The resulting solution was cooled and filtered through Celite. (The preparation was carried out under nitrogen and the solutions were stored under that inert gas.) The THF solutions of lithium tri-*n*-butylborohydride and **3** have a strong, broad absorption in the infrared at 4.95 μ, as has been noted for other alkali metal trialkylborohydrides.[9]

The reductions were carried out by adding 10 mmol of the ketone dissolved in 2.5 ml of THF to 12.5 ml of a 0.8 *M* solution of the borohydride in THF at 0°. After 30 min at 0°, the reaction mixture was treated with 5 ml of 3 *M* sodium hydroxide, followed by 5 ml of 30% hydrogen peroxide. The aqueous phase was saturated with potassium carbonate and the THF layer analyzed by glpc for the isomeric alcohols. In all cases the reactions were complete and no evidence for residual ketone was observed.

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[6] H. C. Brown and D. B. Bigley, *J. Amer. Chem. Soc.*, **83**, 3166 (1961).

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[8] J. Klein, E. Dunkelblum, E. L. Eliel, and Y. Senda, *Tetrahedron Lett.*, 6127 (1968).

[9] P. Binger, G. Benedikt, G. W. Rotermund, and R. Köster, *Ann. Chem.*, **717**, 21 (1968), and references therein.

[10] Allied Chemical Corporation Fellow at Purdue University, 1968–1969.

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Inhibition of the Reaction of Organoboranes with α,β-Unsaturated Carbonyl Derivatives by Galvinoxyl. Evidence for a Free-Radical Chain Mechanism

Sir:

We wish to report that the presence of 5 mol % of galvinoxyl completely inhibits the otherwise fast reactions of organoboranes with acrolein, methyl vinyl ketone, and related α,β-unsaturated carbonyl derivatives. Consequently, these facile 1,4-addition reactions must involve a free-radical chain mechanism.

The facile reaction of organoboranes with α,β-unsaturated carbonyl derivatives, such as methyl vinyl ketone[1] (1), acrolein[2] (2), α-methylacrolein[3] (3), α-bromoacrolein[3] (4), and 2-methylenecyclanones[4] (5), offers a convenient synthesis of a wide variety of substituted aldehydes and ketones.

$$R_3B + CH_2{=}CHCOCH_3 + H_2O \longrightarrow RCH_2CH_2COCH_3 + R_2BOH \tag{1}$$

$$R_3B + CH_2{=}CHCHO + H_2O \longrightarrow RCH_2CH_2CHO + R_2BOH \tag{2}$$

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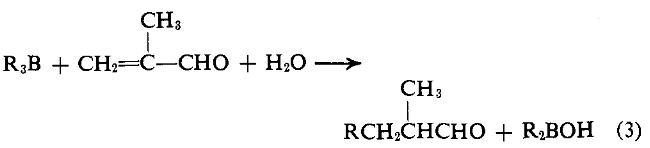
[1] A. Suzuki, A. Arase, H. Matsumoto, M. Itoh, H. C. Brown, M. M. Rogić, and M. W. Rathke, *J. Amer. Chem. Soc.*, **89**, 5708 (1967).

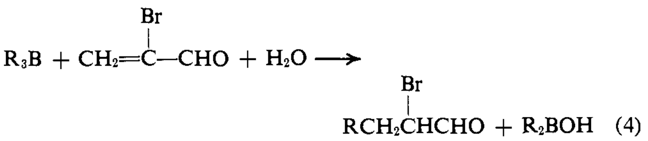
[2] H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **89**, 5709 (1967).

[3] H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **90**, 4165 (1968).

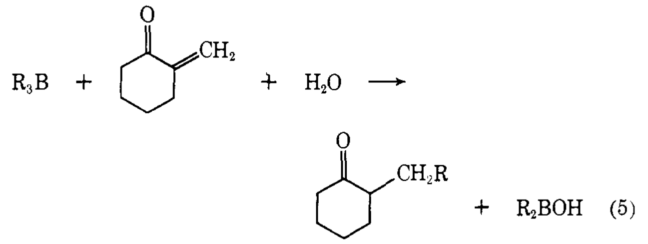
[4] H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **90**, 4165 (1968).



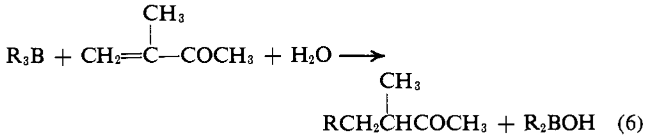
$$R_3B + CH_2{=}\overset{CH_3}{\overset{|}{C}}{-}CHO + H_2O \longrightarrow RCH_2\overset{CH_3}{\overset{|}{C}}HCHO + R_2BOH \quad (3)$$



$$R_3B + CH_2{=}\overset{Br}{\overset{|}{C}}{-}CHO + H_2O \longrightarrow RCH_2\overset{Br}{\overset{|}{C}}HCHO + R_2BOH \quad (4)$$



In exploring the scope of this useful new reaction, we observed that isopropenyl methyl ketone reacts normally (eq 6 and Table I).



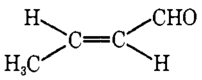
$$R_3B + CH_2{=}\overset{CH_3}{\overset{|}{C}}{-}COCH_3 + H_2O \longrightarrow RCH_2\overset{CH_3}{\overset{|}{C}}HCOCH_3 + R_2BOH \quad (6)$$

Table I. Conversion of Olefins into 3-Methyl-4-alkyl-2-butanones by Reaction of the Corresponding Organoboranes with Isopropenyl Methyl Ketone[a]

Organoborane from olefin[b]	Yield of product, %[c]	Product[d]
1-Pentene	96	73% 3-methyl-2-nonanone
		27% 3,5-dimethyl-2-octanone
1-Hexene	78	83% 3-methyl-2-decanone
		17% 3,5-dimethyl-2-nonanone
1-Octene	77	88% 3-methyl-2-dodecanone
		12% 3,5-dimethyl-2-undecanone
Cyclopentene	88	100% 3-methyl-4-cyclopentyl-2-butanone
Cyclohexene	100	100% 3-methyl-4-cyclohexyl-2-butanone

[a] Reaction conditions: 2 hr at 20° in THF. [b] The authors are indebted to the Phillips Petroleum Company, Bartlesville, Okla., for a generous gift of pure olefins which facilitated this study. [c] By glpc analysis. [d] All products were either compared with authentic samples or exhibited analytical and spectral data in accordance with the assigned structures.

However, *trans*-crotonaldehyde (**1**), *trans*-3-penten-2-one (**2**), mesityl oxide (**3**), 2-cyclohexen-1-one (**4**), and 1-cyclohexenyl methyl ketone (**5**) failed to react under the standard conditions. In some cases we maintained these ketones (**1**–**5**) with triethylborane in tetrahydrofuran or diglyme at 25, 75, and 125° for up to 24 hr without observing any significant reaction. This is in marked contrast to the reactive ketones (eq 1–6), which generally react within a few minutes at 25°.



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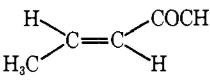

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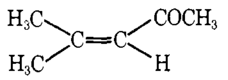

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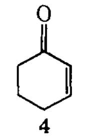

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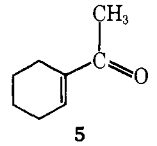
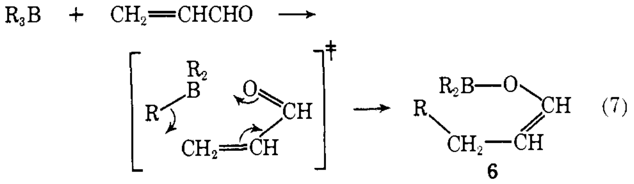


5

The 1,4 addition of the Grignard reagent to α,β-unsaturated ketones is believed to proceed through a cyclic transition state.[5] At one time we considered such a cyclic mechanism for the 1,4 addition of the organoboranes (eq 7). In the absence of water, or other protonolyzing species, the reaction product is the enol borinate[1,2] **6**. This is rapidly hydrolyzed to the product aldehyde (or ketone) by addition of water to the reaction mixture or by carrying the reaction out in the presence of water. The established formation of an enol borinate as the first reaction product would be consistent with such a cyclic addition mechanism.



The failure of mesityl oxide (**3**) to react is readily explicable in terms of such a mechanism. The two methyl groups in **3** could hinder the approach of the incoming alkyl group to the β position. On the other hand, there appeared to be no reason why the single methyl or methylene group in **1**, **2**, and **5** should interfere so seriously with the formation of the cyclic transition state as to effectively prevent reaction under the wide range of conditions explored. Consequently, we were led to explore alternative reaction paths.

The copper-catalyzed 1,4 addition of Grignard reagents[6,7] and the 1,4 addition of copper alkyls or stabilized complexes[8,9] appears to involve a very fast reaction which cannot proceed through a cyclic transition state.[10] Indeed, it has been proposed that these additions proceed through a radical anion process.[10] Accordingly, we began to consider the possibility of a free-radical mechanism for the organoborane reactions.

Galvinoxyl, an efficient scavenger for free radicals,[11] has been used successfully to inhibit extremely fast free-radical chain reactions of organoboranes.[12,13] Indeed, we observed that the addition of 5 mol % of galvinoxyl effectively stops the otherwise very fast 1,4 addition of trialkylboranes to acrolein and to methyl vinyl ketone.

The reactions were carried out as follows. A 25-ml flask fitted with an inlet carrying a rubber serum cap, a magnetic stirring bar, and a condenser was flushed with nitrogen. In the flask was placed 10 mmol (1.42 ml) of triethylborane in 10 ml of diglyme. Then 10 mmol (0.18 ml) of water was added, followed by 20 mmol (1.32 ml) of acrolein. The solution was stirred for 15 min at 25°. Glpc analysis after 15 min indicated that 9.4 mmol (94% yield) of pentanal was present. The reac-

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(5) R. E. Lutz and W. G. Reveley, *J. Amer. Chem. Soc.*, **63**, 3184 (1941).

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(9) E. J. Corey and G. Posner, *J. Amer. Chem. Soc.*, **90**, 5615 (1968).

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(11) P. D. Bartlett and T. Funahashi, *J. Amer. Chem. Soc.*, **84**, 2596 (1962).

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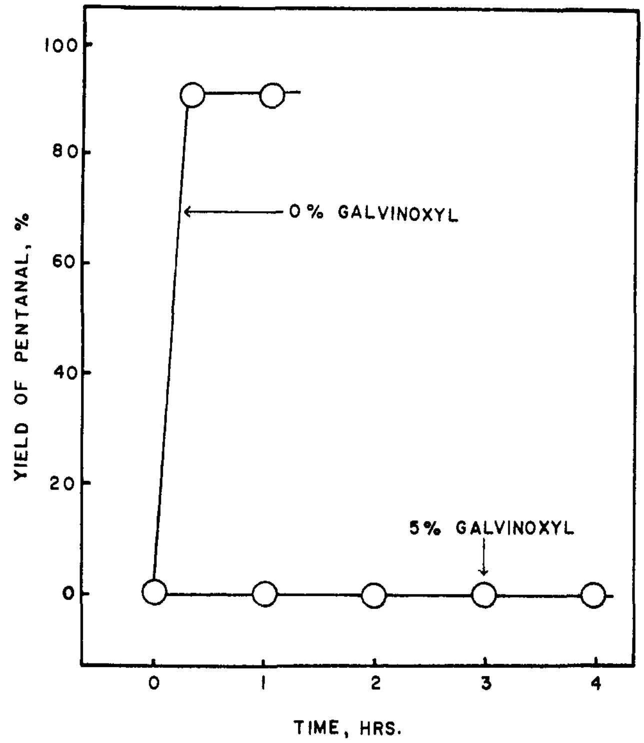

Figure 1. Reaction of acrolein (2.0 *M*) with triethylboron (1.0 *M*) in diglyme at 25°. The effect of added galvinoxyl (in mol %).

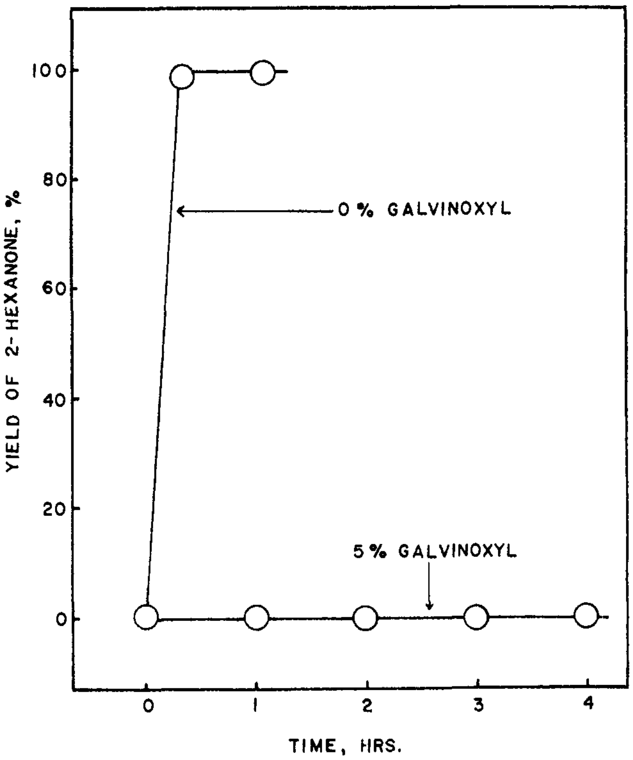

Figure 2. Reaction of methyl vinyl ketone (2.0 *M*) with triethylboron (1.0 *M*) in diglyme at 25°. The effect of added galvinoxyl (in mol %).

tion was then repeated, except that 0.5 mmol (0.21 g) of galvinoxyl was added to the organoborane just prior to the addition of the acrolein. Glpc analysis revealed that no pentanal had formed even after 12 hr, and that the reaction mixture contained 10 mmol of triethylborane and 19 mmol of acrolein.

The results of these studies are shown graphically in Figures 1 and 2.

Consequently, the 1,4 addition of trialkylboranes to α,β-unsaturated carbonyl compounds must be a radical-chain reaction. The mechanism evidently proceeds through the addition of a radical to the carbon–carbon double bond of the carbonyl compound (eq 8), producing a radical intermediate 7. In the absence of a reactive organoborane this intermediate would add to the monomer through carbon to initiate a typical vinyl polymerization.[14] However, in the presence of free trialkylborane, this intermediate (7) evidently reacts through the oxygen atom to form the enol borinate with its very strong boron–oxygen bond (eq 9).[15] This enol borinate then hydrolyzes to form the desired product.

$$\begin{tikzcd}[row sep=small] R\cdot + CH_2{=}CHCHO \arrow[r] & RCH_2\dot{C}HCHO \arrow[d, leftrightarrow] \\ & \underset{7}{RCH_2CH{=}CHO\cdot} \end{tikzcd} \qquad (8)$$

$$7 + R_3B \longrightarrow RCH_2CH{=}CHOBR_2 + R\cdot \qquad (9)$$

Evidently the kinetic chain length for the addition of a free radical to a terminal unsubstituted grouping (A) is much longer than for the corresponding addition to the substituted grouping (B). Consequently, the reactions of organoboranes with the derivatives which contain such an unsubstituted grouping (eq 1–6) proceed spontaneously, or are catalyzed by the presence of mere traces of catalysts, whereas the substituted derivatives (**1–5**) fail to react under the same conditions. Indeed, when triethylborane was added to a reaction mixture containing both methyl vinyl ketone and *trans*-3-penten-2-one (**2**), the methylvinyl ketone reacted, but the *trans*-3-penten-2-one remained essentially unchanged. Fortunately, we have discovered means of catalyzing the reaction of such molecules which fail to undergo the apparent spontaneous reactions 1–6.[16]

$CH_2{=}\overset{|}{C}{-}\overset{|}{C}O$ A $CH(CH_3){=}\overset{|}{C}{-}\overset{|}{C}O$ B

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(14) F. J. Welch, *J. Polymer Sci.*, **61**, 243 (1962).

(15) A. G. Davies and B. P. Roberts, *Chem. Commun.*, 699 (1969), have shown by esr that alkoxy radicals can displace an alkyl radical from a boron center, a reaction analogous to reaction 9. See also, P. J. Krusic and J. K. Kochi, *J. Amer. Chem. Soc.*, **91**, 3944 (1969).

(16) H. C. Brown and G. W. Kabalka, *ibid.*, **92**, 712, 714 (1970).

(17) Graduate research assistant on Grant GM 10937 from the National Institutes of Health.

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The Acyl Peroxide and Photochemical Induced Reactions of Organoboranes with the Inert α,β-Unsaturated Carbonyl Derivatives

Sir:

Trialkylboranes undergo a remarkably fast, spontaneous addition to many α,β-unsaturated carbonyl