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A CONVENIENT SYNTHESIS OF α-BROMOKETONES FROM VINYLOXYBORANES OBTAINED BY THE REACTION OF ORGANOBORANES WITH α,β-UNSATURATED KETONES[1)]

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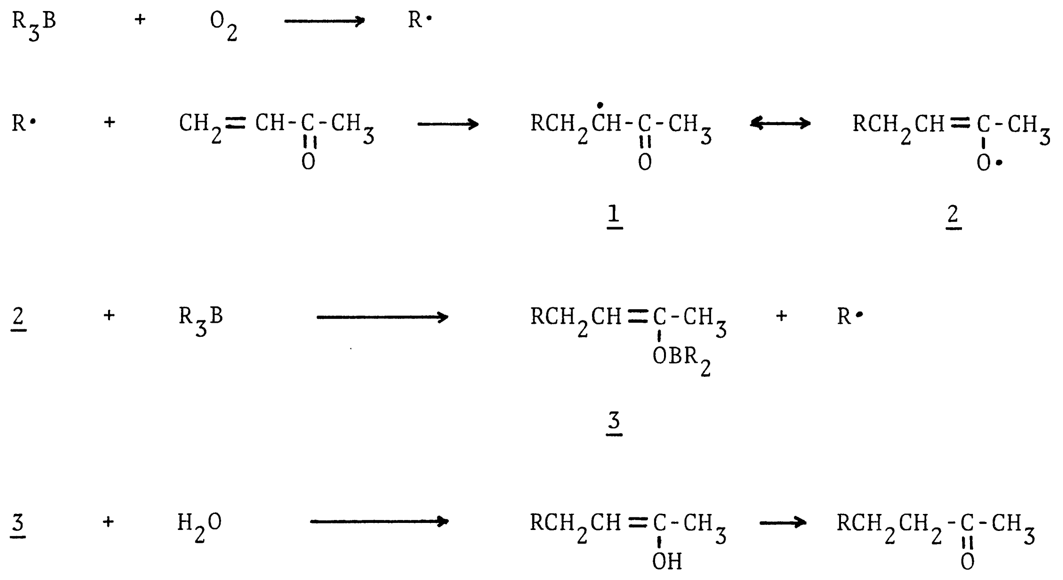
Free-radical addition reaction of organoboranes to α,β-unsaturated ketones forms corresponding vinyloxyboranes (3) as the intermediate. Methanolysis of the dibromoderivatives which should be obtained by bromination of the initially formed vinyloxyboranes provides a convenient one-step synthetic procedure of α-bromoketones from organoboranes in good yields.

We previously reported that organoboranes undergo a spontaneous addition reaction in the presence of oxygen to numerous carbonyl compounds including methyl vinyl ketone,[2)] methyl isopropenyl ketone,[3)] acetylacetylene,[4)] 1,3-butadiene monoxide,[5)] formaldehyde[6)] and 3,4-epoxy-1-butyne,[7)] and that these reactions proceed through a radical chain mechanism since they are promoted by free radical initiators, and are inhibited by radical scavengers such as galvinoxyl and copper N,N-diethyldithiocarbamate. Thus, 1,4-addition of organoboranes to methyl vinyl ketone is readily and conveniently achieved by introducing small quantities of oxygen into the reaction mixture (eq. 1). Hydrolysis of the initially formed intermediate, vinyloxyborane (3), seems to produce corresponding saturated ketone.

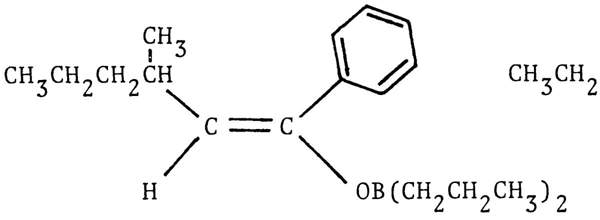
Recently, it has been reported that vinyloxyboranes prepared by various procedures have remarkable potentialities for organic synthesis. For example, Pasto and his co-workers[8)] described the position-specific preparation of dialkylated ketones *via* vinyloxyboranes derived from diazoketones. Mukaiyama et al.,[9)]



$$
\begin{aligned}
&R_3B + O_2 \longrightarrow R\cdot \\
&R\cdot + CH_2{=}CH{-}\underset{\underset{O}{\|}}{C}{-}CH_3 \longrightarrow \underset{\underline{1}}{RCH_2\dot{C}H{-}\underset{\underset{O}{\|}}{C}{-}CH_3} \longleftrightarrow \underset{\underline{2}}{RCH_2CH{=}\underset{\underset{O\cdot}{|}}{C}{-}CH_3} \\
&\underline{2} + R_3B \longrightarrow \underset{\underline{3}}{RCH_2CH{=}\underset{\underset{OBR_2}{|}}{C}{-}CH_3} + R\cdot \qquad (1) \\
&\underline{3} + H_2O \longrightarrow RCH_2CH{=}\underset{\underset{OH}{|}}{C}{-}CH_3 \longrightarrow RCH_2CH_2{-}\underset{\underset{O}{\|}}{C}{-}CH_3
\end{aligned}
$$

reported convenient syntheses of β-hydroxyalkanethioates and β-iminothiol esters by the reaction of ketones and nitriles with a vinyloxyborane formed from thioboronite and ketene. Hooz and Bridson[10)] reported that although α-bromo- and α-chloroketones may be synthesized by treatment of such vinyloxyboranes with N-bromo- or N-chlorosuccinimide, the reaction with molecular bromine gives a rather complex mixture from which only low yields of α-bromocarbonyl compounds can be isolated. We wish to report here that the reaction of molecular bromine with vinyloxyboranes is facilitated by the use of carbon tetrachloride as a solvent and provides a convenient procedure of α-bromocarbonyl compounds.

Although we had previously anticipated the existence of vinyloxyborane (3) from the nmr spectrum,[11)] isolation was not achieved. In this experiment, it was found that such intermediates are readily isolated by distillation under reduced pressure, as described by Pasto and Wojtkowski.[12)] For instance, distillation of the reaction mixture of tri-n-propylborane and methyl vinyl ketone gave a viscous liquids, n_D 1.4340, b.p. 62°C/0.5 mmHg, the elemental analysis of which coincided with that of $C_{13}H_{27}OB$. The infrared spectrum showed absorption bands at 3015 and 1680 cm^{-1} due to the -CH=CH-structure and no absorption in the carbonyl region. The nmr absorption of the vinyl proton of 3 centered at δ 4.50 splits into triplet with J=7.5 Hz, and the remainder of the spectrum was in excellent agreement wit the assigned structure. Similarly, the reaction of tri-n-propylborane with phenyl propenyl ketone in THF produced a mixture of 4 and 5. The nmr spectrum displayed two doublets due to the vinyl hydrogen of 4 and 5 at δ 5.17 with J=8.5 Hz and δ 5.25 with J=8.5 Hz in a relative intensity of 4:1, respectively.



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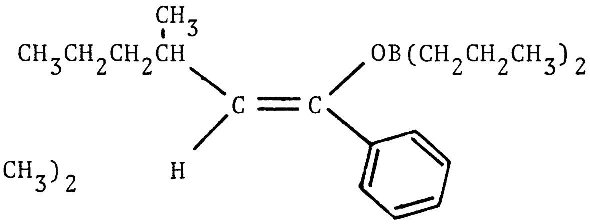

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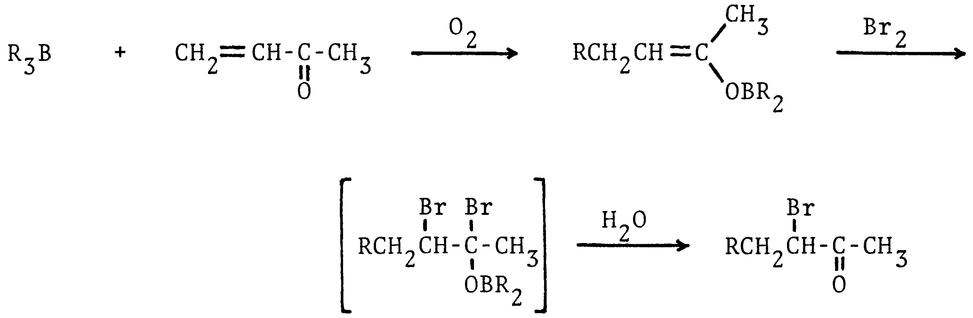
Then, it was indicated that the vinyloxyboranes thus obtained are useful intermediates for the synthesis of α-bromoketones. For instance, when the vinyloxyborane prepared from tri-s-butylborane and methyl vinyl ketone was subjected to bromination at $0^{o}C$ in the dark in CCl_4 and then to methanolysis, 3-bromo-5-methyl-2-heptanone was produced in a yield of 85% (eq. 2). The experimental results are summarized in Table 1.



(2)

The following procedure for the preparation of 3-bromo-5-methyl-2-heptanone is representative. A dry 25-ml flask, equipped with a septum inlet, reflux condenser and magnetic stirrer, was flushed with nitrogen. The flask was charged with 0.6 ml (7.26 mmol) of methyl vinyl ketone and 4 ml (4.84 mmol) of tri-s-butylborane in THF. Under stirring at room temperature, 15 ml of air was passed into the flask at a rate of 1 ml/min through a syringe needle inserted through the rubber septum cap to a point just above the reaction mixture. After removal of THF under reduced pressure, 3 ml of carbon tetrachloride was added. Then, bromine (0.3 ml, 5.80 mmol) was gradually added into the solution in the dark at $0^{o}C$, and the solution was allowed to stir for 30 min at room temperature. Then, 0.3 ml of methanol was added under a slightly reduced pressure in order to remove the hydrogen bromide gas formed, and the mixture was stirred for 1 hr. The solution was analyzed by nmr using benzene as the internal standard. Analysis indicated

Table 1. α-Bromoketones Produced by Bromination of the Vinyloxyboranes Obtained from Representative Organoboranes and α,β-Unsaturated Ketones (eq. 2).

R_3B	α,β-Unsatd. ketone[a]	Product[b]	Yield, %[c]
n-Pr_3B	MVK	3-Bromo-2-heptanone	78
n-Bu_3B	MVK	3-Bromo-2-octanone	74
s-Bu_3B	MVK	3-Bromo-5-methyl-2-heptanone	85
iso-Bu_3B	MVK	3-Bromo-6-methyl-2-heptanone	56
n-Bu_3B	MIPK	3-Bromo-3-methyl-2-octanone	98
s-Bu_3B	MIPK	3-Bromo-3,5-dimethyl-2-heptanone	94

a) MVK=Methyl vinyl ketone, MIPK=Methyl isopropenyl ketone.

b) All products exhibited analytical data and spectra in accordance with the assigned structures.

c) Based on organoborane used.

that 4.12 mmol (a yield of 85%) of 3-bromo-5-methyl-2-heptanone had been formed.

Thus, this new reaction appears to have a wide generality and provides a convenient one-step α-bromoketone synthesis from organoboranes. However, α-bromoaldehydes were not yielded from the vinyloxyboranes which were prepared by the reaction of organoboranes with α,β-unsaturated aldehydes.

We also examined the feasibility of this bromination reaction to intermediates obtained from organoboranes and ethyl diazoacetate.13) It is well known that in spite of the fact that α,β-unsaturated ketones and aldehydes readily react with organoboranes in the presence of oxygen to produce the corresponding saturated ketones and aldehydes, α,β-unsaturated esters give polymers, instead of saturated esters.14) Consequently, the present reaction, if successful, is useful as a convenient one-step synthetic procedure of α-alkyl-α-bromoacetates from organoboranes.

Intermediates produced from organoboranes and ethyl diazoacetate were treated directly with bromine and then methanolyzed by the same procedure described above. Again, the reaction proceeded smoothly and produced the corresponding α-bromoesters in excellent yields, as shown in Table 2.

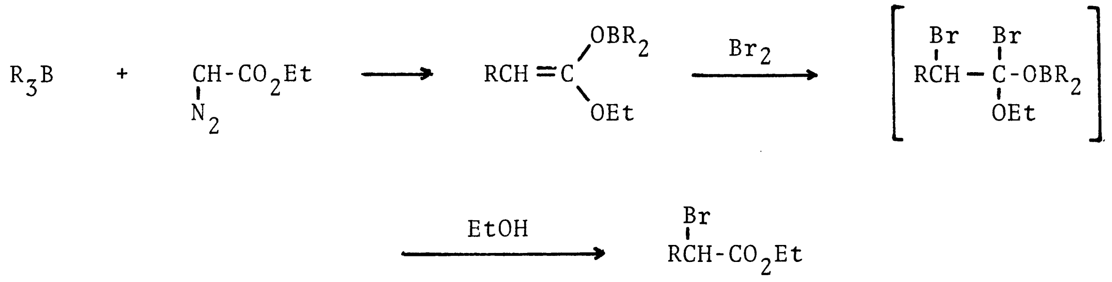
Table 2. α-Bromoesters Produced by Bromination of the Vinyloxyboranes Obtained from Organoboranes and Ethyl Diazoacetate (eq. 3).

R_3B	α-Bromoester[a]	Yield, %[b]
Et_3B	Ethyl α-bromobutyrate	83
n-Bu_3B	Ethyl α-bromocaproate	76

a) Products were identified by direct comparison with authentic samples.

b) Based on organoborane used.

This reaction seems to be considered to proceed through eq. 3.



$$R_3B + \underset{N_2}{CH}\text{-}CO_2Et \longrightarrow RCH{=}C\begin{matrix}OBR_2\\OEt\end{matrix} \xrightarrow{Br_2} \left[\overset{Br}{RCH}-\underset{OEt}{\overset{Br}{C}}\text{-}OBR_2 \right] \xrightarrow{EtOH} \overset{Br}{RCH}\text{-}CO_2Et \qquad (3)$$

The present development adds an interesting application to promising new organic syntheses using the vinyloxyborane intermediate from organoborane. We are actively exploring in an attempt to find such synthetically useful synthetic procedures.

REFERENCES

1) Presented in part at the 20th Symposium on Organometallic Chemistry of the Chemical Society of Japan, Kyoto, October 21, 1972.

2) 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).

3) G. W. Kabalka, H. C. Brown, A. Suzuki, S. Honma, A. Arase, and M. Itoh, ibid., 92, 710 (1970).

4) A. Suzuki, S. Nozawa, M. Itoh, H. C. Brown, G. W. Kabalka, and G. W. Holland, ibid., 92, 3503 (1970).

5) A. Suzuki, N. Miyaura, M. Itoh, H. C. Brown, G. W. Holland, and E. Negishi, J. Amer. Chem. Soc., 93, 2792 (1971).

6) N. Miyaura, M. Itoh, A. Suzuki, H. C. Brown, M. M. Midland, and P. Jacob, ibid., 94, 6549 (1972).

7) A. Suzuki, N. Miyaura, M. Itoh, H. C. Brown, and P. Jacob, Synthesis, 305 (1973).

8) D. J. Pasto and P. W. Wojtkowski, J. Org. Chem., 36, 1790 (1971).

9) T. Mukaiyama, K. Inomata, and M. Muraki, J. Amer. Chem. Soc., 95, 967 (1973).

10) J. Hooz and J. N. Bridson, Can. J. Chem., 50, 2387 (1972).

11) A. Suzuki, S. Honma, A. Arase, and M. Itoh, Abstracts of the 6th Symposium on Oil Chem., Nagoya, p. 54 (1967).

12) D. J. Pasto and P. W. Wojkowski, Tetrahedron Letters, 215 (1970).

13) J. Hooz and S. Linke, J. Amer. Chem. Soc., 90, 6891 (1968).

14) A. Suzuki, A. Arase, S. Honma, and M. Itoh, unpublished work.

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