isomer such strains will be diminished[9] as both the phenyl and *p*-nitrobenzoate groups rotate away from the crowded environment (IX).

In the past high *exo*:*endo* rate ratios in bicyclic systems have invariably been interpreted in terms of $\sigma$ participation in the *exo* isomers. It should now be clear that we can achieve even higher *exo*:*endo* rate ratios in bicyclic systems in derivatives where $\sigma$ participation cannot be significant. Consequently, it becomes necessary to consider each case individually in order to decide whether the observed *exo*:*endo* rate ratio is indeed the result of $\sigma$ participation or whether it is the result of the operation of steric effects.

(9) By introducing methyl groups into the norbornyl system at appropriate positions to alter such strains, it proved possible to change the *exo*:*endo* rate ratio from 885 observed in the parent 2-methyl-2-norbornyl *p*-nitrobenzoates to a low of 6.1 for the 7,7-dimethyl derivative and to a high of 3,630,000 for the 6,6-dimethyl derivative: H. C. Brown and S. Ikegami, *J. Am. Chem. Soc.*, 90, 7122 (1968); S. Ikegami, D. L. Vander Jagt, and H. C. Brown, *ibid.*, 90, 7124 (1968).

(10) National Science Foundation Cooperative Fellow, 1965–1967.

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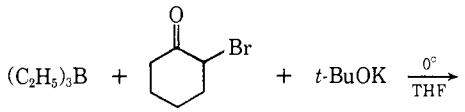
*Received August 9, 1969*

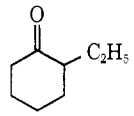
## Reaction of Organoboranes with Bromoacetone under the Influence of Potassium 2,6-Di-*t*-butylphenoxide. A Convenient Procedure for the Conversion of Olefins into Methyl Ketones *via* Hydroboration

*Sir:*

We previously reported that trialkylboranes react with representative $\alpha$-bromo ketones under the influence of potassium *t*-butoxide in tetrahydrofuran, providing the corresponding $\alpha$-monoalkylated ketones in good yields[1,2] (eq 1–3).

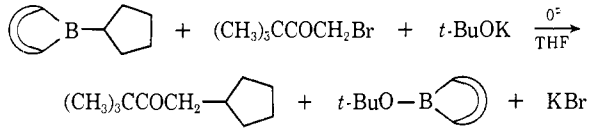


$$(C_2H_5)_3B + \text{(cyclohexanone, 2-Br)} + t\text{-BuOK} \xrightarrow[\text{THF}]{0^\circ}$$

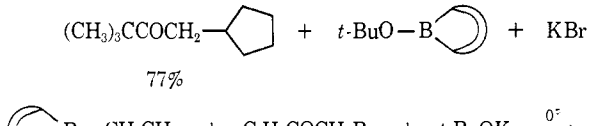


$$+ t\text{-BuOB}(C_2H_5)_2 + KBr \quad (1)$$

68%

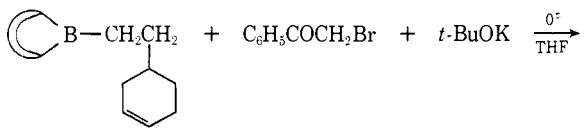


$$\text{(B-cyclopentyl)} + (CH_3)_3CCOCH_2Br + t\text{-BuOK} \xrightarrow[\text{THF}]{0^\circ}$$

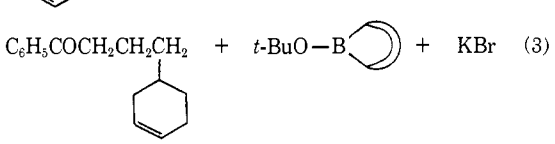


$$(CH_3)_3CCOCH_2\text{-(cyclopentyl)} + t\text{-BuO-B(cyclohexyl)}_2 + KBr \quad (2)$$

77%



$$\text{(B-CH}_2\text{CH}_2\text{-cyclohexyl)} + C_6H_5COCH_2Br + t\text{-BuOK} \xrightarrow[\text{THF}]{0^\circ}$$



$$C_6H_5COCH_2CH_2CH_2\text{-(cyclohexyl)} + t\text{-BuO-B(cyclohexyl)}_2 + KBr \quad (3)$$

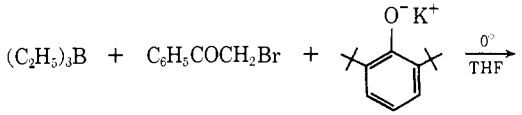
60%

(1) H. C. Brown, M. M. Rogić, and M. W. Rathke, *J. Am. Chem. Soc.*, 90, 6218 (1968).
(2) H. C. Brown, M. M. Rogić, H. Nambu, and M. W. Rathke, *ibid.*, 91, 2147 (1969).

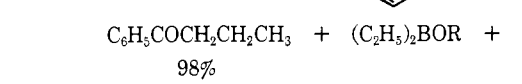
We pointed out that once the reaction had been demonstrated to proceed satisfactorily with a particular $\alpha$-halo ketone, it appeared to proceed satisfactorily with a wide variety of alkyl groups in the form of $R_3B$ or B-R-9-BBN derivatives.[2] Unfortunately, the reaction proved to be quite sensitive to the structure of the $\alpha$-halo ketone, and all our attempts to extend it to $\alpha$-bromoacetone failed. This was especially disappointing because the successful alkylation of this derivative would provide a new, highly convenient synthesis of methyl ketones, very useful synthetic intermediates.

It appeared to us that the difficulty might lie in the use of potassium *t*-butoxide as the base. This is an exceptionally strong base, and $\alpha$-halo ketones are extraordinarily sensitive to the action of such bases.[3] Accordingly, we decided to screen a large number of bases, using the reaction of phenacyl bromide and triethylborane as a model system. Although a number of promising bases were discovered, the most satisfactory proved to be 2,6-di-*t*-butylphenoxide, a base which does not appear to have been previously utilized for condensation reactions in organic chemistry.

Presence of the large alkyl substituents in the *ortho* positions appears to be highly favorable for the desired reaction. Thus the yield of product (*n*-butyrophenone) was 2% with potassium phenoxide, 24% with the 2-methyl derivative, 75% with the 2,6-dimethyl, and 98% with the 2,6-di-*t*-butyl compound (eq 4). Possi-



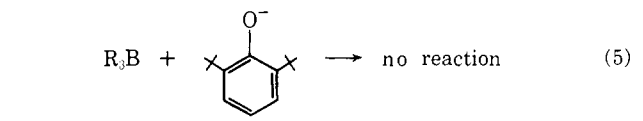
$$(C_2H_5)_3B + C_6H_5COCH_2Br + \text{(O}^-\text{K}^+\text{-2,6-di-t-Bu-C}_6\text{H}_3\text{)} \xrightarrow[\text{THF}]{0^\circ}$$



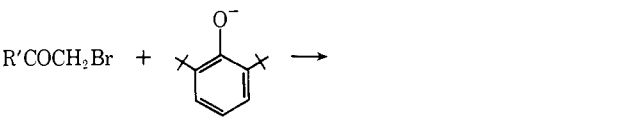
$$C_6H_5COCH_2CH_2CH_3 + (C_2H_5)_2BOR + KBr \quad (4)$$

98%

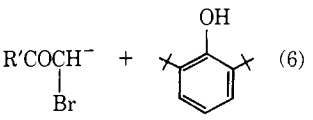
bly, the bulky substituents prevent the organoborane from coordinating with the base (eq 5). Consequently, when the base acts on the $\alpha$-halo ketones to produce the $\alpha$-halo carbanion (eq 6), the latter is immediately removed by reaction with the free, uncomplexed organo-



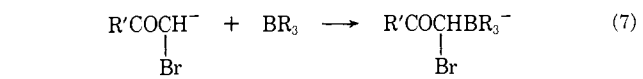
$$R_3B + \text{(O}^-\text{-2,6-di-t-Bu-C}_6\text{H}_3\text{)} \longrightarrow \text{no reaction} \quad (5)$$



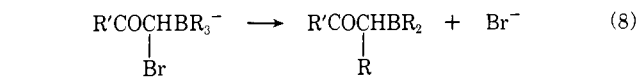
$$R'COCH_2Br + \text{(O}^-\text{-2,6-di-t-Bu-C}_6\text{H}_3\text{)} \longrightarrow$$



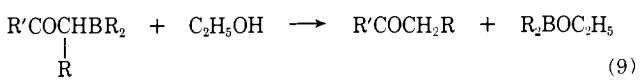
$$R'\underset{\underset{Br}{|}}{COCH^-} + \text{(OH-2,6-di-t-Bu-C}_6\text{H}_3\text{)} \quad (6)$$



$$R'\underset{\underset{Br}{|}}{COCH^-} + BR_3 \longrightarrow R'\underset{\underset{Br}{|}}{COCHBR_3^-} \quad (7)$$



$$R'\underset{\underset{Br}{|}}{COCHBR_3^-} \longrightarrow R'\underset{\underset{R}{|}}{COCHBR_2} + Br^- \quad (8)$$



$$R'\underset{\underset{R}{|}}{COCHBR_2} + C_2H_5OH \longrightarrow R'COCH_2R + R_2BOC_2H_5 \quad (9)$$

(3) See H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, for a discussion of the use of various bases for condensations, with pertinent literature references.

borane (eq 7). Following transfer of the alkyl group from boron (eq 8), the product is obtained by hydrolysis of the intermediate (eq 9).

Of considerable importance is the observation that this base is so mild that representative ketones can exist in its presence for a considerable time without undergoing significant change. For example, 0.5 *M* solutions of acetone, acetophenone, and cyclohexanone were treated with an equivalent amount of potassium 2,6-di-*t*-butylphenoxide at 25° and the mixtures analyzed by glpc. No significant change in the concentration of the ketones was observed over 24 hr. On the other hand, the use of potassium *t*-butoxide at 0° resulted in the immediate disappearance of the ketones.

In the previous procedure[1,2] it was necessary to add the potassium *t*-butoxide to a mixture of the organoborane and α-halo ketone, being careful to avoid any excess of the base. However, with potassium 2,6-di-*t*-butylphenoxide it proved satisfactory to have it present in the reaction mixture with the organoborane, completing the reaction by the slow addition of the α-halo ketone. An excess of base has no apparent effect. Even more convenient, the base can be synthesized *in situ* by adding to the organoborane solution in THF the proper quantity of 2,6-di-*t*-butylphenol followed by a solution of potassium *t*-butoxide in the same solvent. The reaction is then completed by introducing the α-halo ketone. The hindered phenol formed in the reaction mixture is evidently slow to protonolyze the intermediate, so that ethanol is added to liberate the product (eq 9).

Far more important than these obvious conveniences is the fact that this base makes possible the successful alkylation of α-bromoacetone, making available a highly convenient route to a wide variety of methyl ketones[4] (eq 10, 11). Utilizing this base we have also successfully achieved the alkylation of chloroacetonitrile, providing a convenient new route to nitriles,[5] and, surprising in view of the mildness of the base, have successfully accomplished the rapid reaction of organoboranes with the α-halo esters.[6]

$$n\text{-Bu}_3\text{B} + \text{CH}_2\text{BrCOCH}_3 \longrightarrow n\text{-BuCH}_2\text{COCH}_3 \quad (10)$$
84%

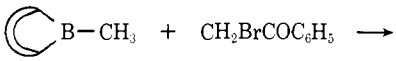
(11)

73%

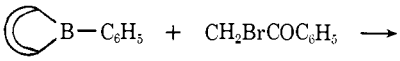
These alkylations can be achieved either with trialkylboranes or B-alkyl-9-borabicyclo[3.3.1]nonanes[7] available *via* hydroboration. In addition we established that it was possible to use the new B-methyl-9-BBN and B-phenyl-9-BBN reagents[8] (eq 12–15).

The results realized in the alkylation of α-bromoacetone are summarized in Table I.

The following procedure is illustrative. In a dry 500-ml flask equipped with a septum inlet, pressure-equalizing dropping funnel, condenser, and magnetic stirrer was placed 3.9 g (100 mg-atoms) of potassium. The flask was flushed with nitrogen and a solution of


(12)

73%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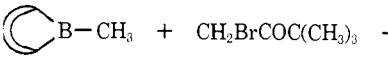
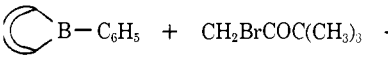
91%


(14)

68%


(15)

90%

24.7 g of 2,6-di-*t*-butylphenol (120 mmoles) in 200 ml of tetrahydrofuran was added at room temperature. Following the initial vigorous reaction, the mixture was refluxed for 1 hr to complete the reaction. The mixture was cooled to 0° and 14.2 ml of triethylboron (100 mmoles) was added, followed by the dropwise addition of 13.7 g (100 mmoles) of α-bromoacetone in 50 ml of tetrahydrofuran. The mixture was then stirred for 30 min and brought to room temperature, and 25 ml of ethanol was added to liberate the product. Glpc examination indicated a yield of 88%. Fractional distillation gave 6.0 g of 2-pentanone, bp 101–102°, an isolated yield of 70%.

**Table I.** α Alkylation and α Arylation of Bromoacetone with Organoboranes under the Influence of Potassium 2,6-Di-*t*-butylphenoxide[a]

| Organoborane $R_3B$ or B-R-9-BBN | Product | Yield,[b] % |
|---|---|---|
| Triethyl | 2-Pentanone | 88[c] |
| Tri-*n*-butyl | 2-Heptanone | 84[c] |
| B-*n*-Butyl | 2-Heptanone | 80 |
| B-2-Butyl | 4-Methyl-2-hexanone | 71 |
| B-Isobutyl | 5-Methyl-2-hexanone | 62 |
| Tricyclopentyl | 1-Cyclopentyl-2-propanone | 43[c] |
| B-Cyclopentyl | 1-Cyclopentyl-2-propanone | 73 |
| B-Cyclohexyl | 1-Cyclohexyl-2-propanone | 72 |
| B-*exo*-Norbornyl | 1-(2-Norbornyl)-2-propanone[d] | 25 |
| B-Phenyl | 1-Phenyl-2-propanone | 76 |

[a] All reactions were carried out in tetrahydrofuran solution at 0° using 10 mmoles each of the organoborane, the base, and the bromoacetone. [b] Glpc analysis after addition of ethanol. [c] Based on the availability of only one alkyl group per trialkylborane molecule. [d] The stereochemistry was not established, but is probably the *exo* isomer from the apparent reaction mechanism.

We tested four different procedures, using phenacyl bromide and triethylborane. Each procedure gave quite satisfactory yields. (A) The base was prepared from potassium and the phenol and mixed with the organoborane, and the α-bromo ketone was added (above procedure); yield 98%. (B) The phenol was added to the organoborane and the base prepared *in situ* by the addition of a solution of potassium *t*-butoxide in THF, followed by the addition of the α-bromo ketone; yield 98%. (C) The procedure was the same as B, but a solution of potassium *t*-butoxide in *t*-butyl alcohol was used to prepare the base; yield 88%. (D) The organoborane, the phenol, and the phenacyl bromide were treated with potassium *t*-butoxide in THF, forming the new base *in situ*; yield 98%.

Consequently, it appears that each of these procedures is effective, so that the choice of the particular procedure

(4) Methyl ketones had been previously synthesized from organoboranes by utilizing the reaction with diazoketones: J. Hooz and S. Linke, *J. Am. Chem. Soc.*, **90**, 6891 (1968).
(5) H. C. Brown, H. Nambu, and M. M. Rogić, *ibid.*, **91**, 6854 (1969).
(6) H. C. Brown, H. Nambu, and M. M. Rogić, *ibid.*, **91**, 6855 (1969).
(7) E. F. Knights and H. C. Brown, *ibid.*, **90**, 5280, 5281 (1968).
(8) H. C. Brown and M. M. Rogić, *ibid.*, **91**, 4304 (1969).

to be adopted should depend primarily on convenience in a particular situation.

(9) Visiting scholar on funds provided by the Mitsui Petrochemical Industries, Ltd., Tokyo, Japan.

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## Reaction of Organoboranes with Chloroacetonitrile under the Influence of Potassium 2,6-Di-*t*-butylphenoxide. A Convenient Procedure for the Conversion of Olefins into Nitriles *via* Hydroboration

*Sir:*

Trialkylboranes react, under the influence of potassium *t*-butoxide (in *t*-butyl alcohol or tetrahydrofuran), with ethyl haloacetate, ethyl dihaloacetate, and various $\alpha$-halo ketones to give the $\alpha$-alkylacetate[1] (eq 1), the $\alpha$-alkyl-$\alpha$-haloacetate[2] (eq 2), the $\alpha,\alpha$-dialkylacetate[2] (eq 3), and the corresponding $\alpha$-alkyl ketones[3,4] (eq 4).

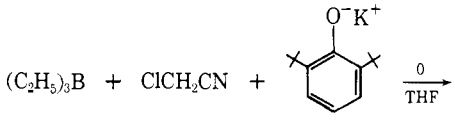
$$R_3B + CH_2XCO_2C_2H_5 \xrightarrow[t\text{-BuOH}]{t\text{-BuOK}} RCH_2CO_2C_2H_5 \quad (1)$$

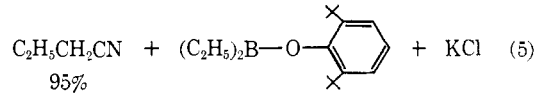
$$R_3B + CHX_2CO_2C_2H_5 \xrightarrow[t\text{-BuOH}]{t\text{-BuOK}} RCHXCO_2C_2H_5 \quad (2)$$

$$2R_3B + CHX_2CO_2C_2H_5 \xrightarrow[t\text{-BuOH}]{2t\text{-BuOK}} R_2CHCO_2C_2H_5 \quad (3)$$

$$R_3B + CH_2XCOR' \xrightarrow[THF]{t\text{-BuOK}} RCH_2COR' \quad (4)$$

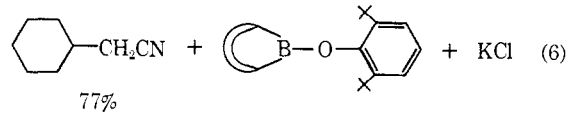
All attempts to extend the reaction to the synthesis of nitriles by a related alkylation of chloroacetonitrile under the influence of potassium *t*-butoxide had been unsuccessful. Our success in achieving the alkylation of bromoacetone under the influence of potassium 2,6-di-*t*-butylphenoxide, a mild base of large steric requirements,[5] encouraged us to try it with chloroacetonitrile. The reaction proved highly satisfactory. Consequently, this alkylation of chloroacetonitrile provides a convenient new synthetic route to nitriles (with addition of a two-carbon moeity to the molecule) and to the various derivatives to which nitriles are readily converted (amines, amides, carboxylic acids) (eq 5, 6).





95%

(5)



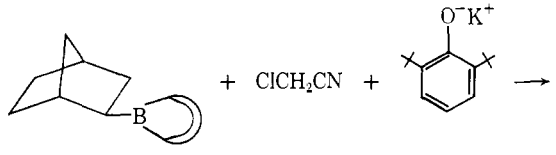
77%

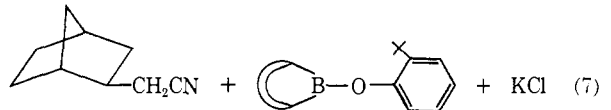
(6)

In the corresponding reaction with bromoacetone[5] it was noted that protonolysis of the reaction intermediate by the 2,6-di-*t*-butylphenol produced in the reaction was relatively difficult. Consequently, ethanol was added to liberate the ketone. However, in the present case the reaction intermediate evidently undergoes protonolysis much more readily, so that examination of the reaction mixture by glpc revealed the presence of the product in high yield without adding ethanol or other protonolyzing agent.

Recently Hooz and Linke have reported that diazoacetone, diazoacetonitrile, and ethyl diazoacetate react with trialkylboranes to yield the corresponding ketones,[6] nitriles,[7] and esters.[7] These reactions provide an important new route to these derivatives.

In all of these reactions only one of the three groups of a trialkylborane is utilized. This limitation could constitute a major difficulty in cases where it is desired to apply these homologation reactions to valuable intermediates. Fortunately, the use of the B-alkyl-9-borabicyclo[3.3.1]nonane derivatives[8] (B-R-9-BBN) circumvented this difficulty for the base-induced synthesis of esters[9] and ketones.[4,5] The same expedient served for the present nitrile synthesis[10] (eq 7).

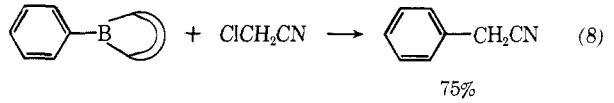




65%

(7)

The new B-aryl-9-BBN reagents[11] also were satisfactory to achieve $\alpha$ arylation of chloroacetonitrile (eq 8). The experimental results are summarized in Table I.



75%

(8)

The procedure is indicated by the preparation of cyclopentylacetonitrile. The apparatus and the prepara-

(1) H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *J. Am. Chem. Soc.*, **90**, 818 (1968).
(2) H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **90**, 1911 (1968).
(3) H. C. Brown, M. M. Rogić, and M. W. Rathke, *ibid.*, **90**, 6218 (1968).
(4) H. C. Brown, M. M. Rogić, H. Nambu, and M. W. Rathke, *ibid.*, **91**, 2147 (1969).
(5) H. C. Brown, H. Nambu, and M. M. Rogić, *ibid.*, **91**, 6852 (1969).
(6) J. Hooz and S. Linke, *ibid.*, **90**, 5936 (1968).
(7) J. Hooz and S. Linke, *ibid.*, **90**, 6891 (1968).
(8) E. F. Knights and H. C. Brown, *ibid.*, **90**, 5280, 5281 (1968).
(9) H. C. Brown and M. M. Rogić, *ibid.*, **91**, 2146 (1969).
(10) We did not attempt to see whether the B-R-9-BBN derivatives would solve this difficulty with diazoacetonitrile. Previously, we had observed that these derivatives did not overcome the problem with ethyl diazoacetate.[9]
(11) H. C. Brown and M. M. Rogić, *J. Am. Chem. Soc.*, **91**, 4304 (1969).