Reaction of Organoboranes with Dichloroacetonitrile under the Influence of Potassium 2,6-Di-*tert*-butylphenoxide. A Convenient General Procedure for the Preparation of α-Chloro Nitriles and Dialkylacetonitriles

Sir:

We wish to report that organoboranes, readily available *via* hydroboration,[1] undergo facile reaction with dichloroacetonitrile under the influence of potassium 2,6-di-*tert*-butylphenoxide to give the corresponding dialkylacetonitriles of α-alkyl-α-chloroacetonitriles in satisfactory yields. Since the reaction can be extended to the introduction of two secondary alkyl groups, it provides a route to the synthesis of dialkylacetic acids more general than the usual malonic acid ester procedure.[2]

We previously reported that the reaction of simple organoboranes[3] or *B*-alkyl-9-borabicyclo[3.3.1]nonanes[4] with ethyl mono- and dihaloacetates, in the presence of potassium *tert*-butoxide, provides a convenient new procedure for the alkylation of these esters. More recently, it was discovered that the base, potassium 2,6-di-*tert*-butylphenoxide, possesses advantages for such alkylations[5] and permits its extension to bromoacetone,[5] chloroacetonitrile,[5] and ethyl 4-bromocrotonate.[6]

The dialkylation of ethyl dihaloacetate offered a promising new route to dialkylacetic acid esters.[3] Unfortunately, such dialkylations proceed in satisfactory yield only with primary alkyl groups. There is no difficulty in introducing secondary alkyl groups in high yield in monoalkylation.[3,4] Consequently, the difficulty in introducing secondary alkyl groups in the dialkylation reaction appeared to have its origin in large steric effects accompanying the coordination of a highly hindered carbanion with the organoborane.

Other studies had indicated that the nitrile grouping is far less sterically demanding than the carbethoxy grouping in such reactions.[7] Accordingly, we undertook a study of the alkylation of dichloroacetonitrile.

Monoalkylation of dichloroacetonitrile was first studied. A procedure which involves the addition of potassium *tert*-butoxide in tetrahydrofuran to an equimolar mixture of an appropriate trialkylborane, dichloroacetonitrile, and 2,6-di-*tert*-butylphenol in the same solvent at 0° proved to be quite satisfactory. Thus 2-chlorobutyronitrile was obtained in 89% yield from triethylborane (eq 1).

$$(C_2H_5)_3B + Cl_2CHCN + 2,6\text{-}tert\text{-}Bu_2C_6H_3OH \xrightarrow{KO\text{-}tert\text{-}Bu} \underset{89\%}{CH_3CH_2CHClCN} \quad (1)$$

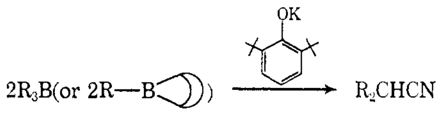
The reaction was applied to a number of organoboranes produced *via* the hydroboration of representative olefins. In all cases the reactions proceed smoothly and satisfactory yields are realized. The results are summarized in Table I.

Table I. Monoalkylation of Dichloroacetonitrile under the Influence of Potassium 2,6-Di-*tert*-butylphenoxide[a]

Organoborane R_3B or *B*-R-9-BBN	Product[b]	Yield,[c] %	Bp, °C (mm)	$n^{20}\text{D}$
Triethyl	2-Chlorobutyronitrile	89	68–70 (60)	1.4192
B-Ethyl	2-Chlorobutyronitrile	87		
B-*n*-Butyl	2-Chlorohexanonitrile	75	67–68 (9)	1.4334
B-Isobutyl	2-Chloro-4-methylpentanonitrile	73	58–61 (9)	1.4295
B-*sec*-Butyl	2-Chloro-3-methylpentanonitrile	69	62–63 (9)	1.4363
B-Cyclopentyl[d]	2-Chloro-2-cyclopentylacetonitrile	76	88–89 (9)	1.4698
B-Cyclohexyl[d]	2-Chloro-2-cyclohexylacetonitrile	78	102–104 (8)	1.4798

[a] All reactions were carried out at 25° for 3 hr. The following addition mode was used: addition of potassium *tert*-butoxide to the mixture of organoborane, dichloroacetonitrile, and the phenol. [b] The structures were confirmed by nmr and ir examination. [c] Analysis by glpc. [d] In these cases, 2,4,6-tri-*tert*-butylphenol was used to facilitate glpc analysis and isolation.

The reaction also is highly satisfactory for the dialkylation of the reagent. By utilizing 2 mol of base and 2 mol of the organoborane, the dialkylacetonitrile with two identical alkyl groups is readily produced (eq 2). Alternatively, the dialkylacetonitrile with two different alkyl groups is readily obtained in two successive monoalkylations (eq 3, 4).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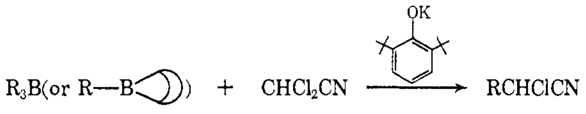
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(4)

Two primary alkyl groups are readily introduced in this way, utilizing the usual mild conditions. Introduction of the more hindered alkyl groups, such as isobutyl, *sec*-butyl, or cyclopentyl, is more sluggish

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[1] H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

[2] A. C. Cope, H. L. Holmes, and H. O. House, *Org. React.*, **9**, 107 (1957).

[3] H. C. Brown and M. M. Rogić, *J. Amer. Chem. Soc.*, **90**, 818, 1911 (1968).

[4] H. C. Brown and M. M. Rogić, *ibid.*, **91**, 2146 (1969).

[5] H. C. Brown, H. Nambu, and M. M. Rogić, *ibid.*, **91**, 6852, 6854, 6855 (1969).

[6] H. C. Brown and H. Nambu, *ibid.*, **92**, 1761 (1970).

[7] H. Nambu and H. C. Brown, *Organometal. Chem. Syn.*, in press.

Table II. Dialkylation of Dichloroacetonitrile and Alkylation of α-Alkyl-α-chloroacetonitriles under the Influence of Potassium 2,6-Di-*tert*-butylphenoxide[a]

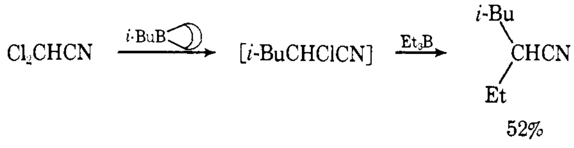
Organoborane, R$_3$B or *B*-R-9-BBN	Chloronitrile, Cl$_2$CHCN or RCH(Cl)CN	Reaction conditions		Product[b]	Yield,[c] %	Bp, °C (mm)	$n^{20}\mathrm{D}$
		Temp, °C	Time, hr				
Ethyl	Dichloro	25	3	Diethylacetonitrile	96	40–41 (10)	1.4047
B-Ethyl	Dichloro	25	3	Diethylacetonitrile	97		
B-*n*-Butyl	Dichloro	25	3	Di-*n*-butylacetonitrile	85	97–99 (8)	1.4264
B-Isobutyl	Dichloro	Reflux	24	Diisobutylacetonitrile	66	83–85 (7)	1.4210
B-*sec*-butyl	Dichloro	Reflux	24	Di-*sec*-butylacetonitrile	46	88–90 (7)	1.4356
Triethyl	Isobutylchloro	25	3	2-Ethyl-4-methylpentanonitrile	88	58–60 (8)	1.4143
Triethyl	*sec*-Butylchloro	25	3	2-Ethyl-3-methylpentanonitrile	91	67–68 (9)	1.4197
Triethyl[d]	Cyclopentylchloro	25	3	2-Cyclopentylbutyronitrile	83	91–92 (9)	1.4491
Triethyl[d]	Cyclohexylchloro	25	3	2-Cyclohexylbutyronitrile	85	98–100 (7)	1.4617
B-Cyclohexyl[d]	*sec*-Butylchloro	Reflux	24	2-Cyclohexyl-3-methylpentanonitrile	61	98–102 (9)	1.4615
B-Cyclopentyl[d]	Cyclopentylchloro	Reflux	24	Dicyclopentylacetonitrile	56	135–138 (9)	1.4828

[a] All reactions were carried out in tetrahydrofuran–*tert*-butyl alcohol (4:1) solution for facile protonolysis of the reaction intermediate. The following addition mode was used: addition of chloronitriles to the mixture of organoborane and potassium 2,6-di- or 2,4,6-tri-*tert*-butylphenoxides. [b] Their structures were confirmed by nmr and ir examination. [c] Analysis by glpc. [d] In these cases potassium 2,4,6-tri-*tert*-butylphenoxide was used as the base to facilitate glpc analysis and isolation.

and requires reflux in tetrahydrofuran for extended periods of time. In addition, it was noted that the protonolysis of the boron intermediate in such cases is relatively slow, so that a mixed solvent, *tert*-butyl alcohol–THF (1:4), is used to facilitate liberation of the desired product. With these modifications, it has proved possible to extend the reaction to the introduction of two secondary alkyl groups, as in the synthesis of dicyclopentylacetonitrile.

The results for the dialkylation experiments are summarized in Table II.

As a final extension of this reaction, we explored the possibility of achieving the successive dialkylation of dichloroacetonitrile by two different alkyl groups, without isolating the intermediate. The monoalkylation of dichloroacetonitrile was carried out as previously described. To the reaction mixture was added an equimolar quantity of another organoborane, followed by the dropwise addition of potassium *tert*-butoxide in the *tert*-butyl alcohol–THF solution. Typical results are shown in eq 5–8.



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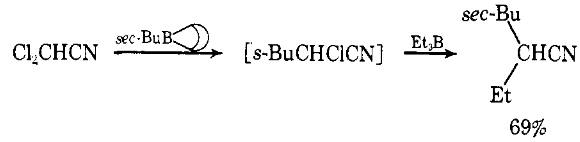

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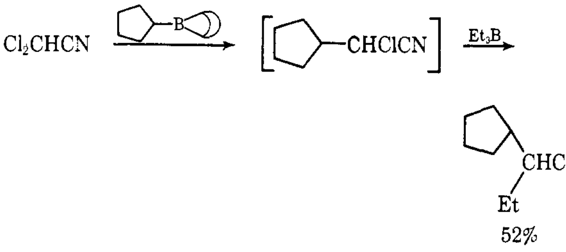

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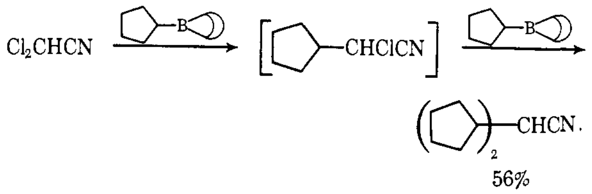

(8)

The following procedure is illustrative. In a dry 200-ml flask, equipped with a septum inlet, a pressure-equalizing dropping funnel, a condenser, and a magnetic stirring bar, was placed 2.88 g (11 mmol) of 2,6-di-*tert*-butylphenol. The flask was flushed with nitrogen and 20 ml of a 1:1 mixture of THF and *tert*-butyl alcohol was introduced. The flask was immersed in an ice–water bath and 1.1 g (10 mmol) of dichloroacetonitrile and 10 mmol of *B*-*sec*-butyl-9-BBN in 15 ml of THF (prepared from 10 mmol of 9-BBN and 10 mmol of *cis*-2-butene) were added at once to the flask, followed by the dropwise addition of potassium *tert*-butoxide (10 mmol) in 11 ml of THF over a period of 10 min. After being stirred for 30 min at the same temperature, the reaction mixture was brought to room temperature and allowed to stir for an additional 3 hr. The flask was then cooled with an ice–water bath. Triethylborane, 1.42 ml (10 mmol), was injected at once into the mixture, followed by the dropwise addition of potassium *tert*-butoxide (10 mmol) in 11 ml of THF for 10 min. The resulting mixture was allowed to stir for 30 min and brought to room temperature. Glpc analysis, following addition of *n*-dodecane as an internal standard, indicated a 69% yield of *sec*-butylethylacetonitrile.

It is evident that the present reaction provides a highly convenient procedure for the synthesis of both α-chloro nitriles and dialkylacetonitriles. Since the dialkylacetonitriles are readily hydrolyzed to carboxylic acids, this provides an alternative to the widely used malonic acid ester synthesis of dialkylacetic acids. A major advantage of the present development for such syntheses is the fact that the synthesis can accommodate the introduction of two secondary alkyl groups.

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(8) Visiting scholar on funds provided by the Mitsui Petro-chemical Industries, Ltd., Tokyo, Japan.

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Received June 11, 1970