Organoborates in Organic Synthesis: The Use of Alkenyl-, Alkynyl-, and Cyano-borates as Synthetic Intermediates

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1 Introduction

It is now twenty-one years since H. C. Brown and Subba Rao demonstrated that alkenes readily react with diborane in the presence of ether solvents to give the corresponding organoboranes in high yield.[1] The ready availability of organoboranes has led to extensive studies of their chemistry and to the development of many reactions of great value in synthetic organic chemistry.[2–4]

Of prime importance in the development of many synthetically useful reactions has been the observation that organoborates, formed by the reaction of organoboranes with appropriately substituted nucleophilic species, tend to undergo spontaneous 1,2-migrations of an organic group from boron to an acceptor atom as illustrated in reactions 1—4.

$$R_3B + {}^{-}O_2H \rightarrow R_3\bar{B}—O—OH \rightarrow R_2B—O—R + {}^{-}OH \qquad (1)$$

$$R_3B + NH_2—OSO_3H \rightarrow R_3\bar{B}—\overset{+}{N}H_2—OSO_3H \rightarrow R_2B—\overset{+}{N}H_2—R + {}^{-}OSO_3H \qquad (2)$$

$$R_3B + \overset{+}{N}_2—\bar{C}HCO_2R^1 \rightarrow R_3\bar{B}—CH(N_2{}^{+})(CO_2R^1) \rightarrow R_2B—CHRCO_2R^1 + N_2 \qquad (3)$$

$$R_3B + \bar{C}\equiv\overset{+}{O} \rightarrow R_3\bar{B}—C\equiv\overset{+}{O} \rightarrow R_2B—COR \qquad (4)$$

The organoborate ions formed in the above reactions are generally formed as transient species which undergo rapid rearrangement. In the absence of a suitable activating group, however, many nucleophiles and bases react with organoboranes to give stable organoborates, which do not undergo further spontaneous reactions. Reaction of some such organoborates with suitable electrophiles can, however, result in synthetically useful transformations, and the application of these reactions has, in recent years, led to the development of many valuable

[1] H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, 1956, **78**, 5694.
[2] H. C. Brown, 'Boranes in Organic Chemistry', Cornell University Press, Ithaca, New York, 1972.
[3] G. M. L. Cragg, 'Organoboranes in Organic Synthesis', Dekker, New York, 1973.
[4] H. C. Brown, 'Organic Syntheses via Boranes', Wiley, New York, 1975.

new synthetic methods.[5] The most useful organoborates studied to date have been the alkenyl-, alkynyl-, and cyano-borates, and it is the object of this review to illustrate the application of these compounds to the synthesis of a variety of organic compounds.

2 Preparation of Alkenyl-, Alkynyl-, and Cyano-borates

Lithium alkenyl-[6] and alkynyl-trialkylborates[7] may be readily prepared by the reaction of the corresponding alkenyl- or alkynyl-lithium reagents with trialkylboranes in an ethereal solvent (reactions 5 and 6).

$$R_3B + LiCH{=}CH_2 \xrightarrow{Et_2O,\ 0°C} [R_3\bar{B}{-}CH{=}CH_2]\,Li^+ \qquad (5)$$

$$R^1{}_3B + LiC{\equiv}CR^2 \xrightarrow{THF,\ 0°C} [R^1{}_3\bar{B}{-}C{\equiv}CR^2]\,Li^+ \qquad (6)$$

Extension of the latter reaction to the preparation of ethynyltrialkylborates (R^2 = H) can be complicated by disproportionation of the product to ethyne and ethynylbis(trialkylborates) (reaction 7).[8]

$$R_3B + NaC{\equiv}CH \xrightarrow[34°C]{Et_2O} [R_3\bar{B}{-}C{\equiv}CH]\,Na^+ \rightarrow [R_3\bar{B}{-}C{\equiv}C{-}\bar{B}R_3]2Na^+ + HC{\equiv}CH \qquad (7)$$

Though lithium ethynyltrialkylborates have been prepared in good yield by reaction of ethynyl-lithium with trialkylborates at −78 °C (reaction 8),[9] the

$$R_3B + LiC{\equiv}CH \xrightarrow{THF,\ -78°C} [R_3\bar{B}{-}C{\equiv}CH]\,Li^+ \qquad (8)$$

danger of disproportionation can be obviated by use of ethynyl-lithium ethylenediamine complex in place of ethynyl-lithium (reaction 9).[10]

$$R_3B + LiC{\equiv}CH{,}EDA \xrightarrow{THF,\ r.t.} [R_3\bar{B}{-}C{\equiv}CH]\,Li^+\,EDA \qquad (9)$$

Alternative routes to lithium[11] and sodium[8] alkynyltrialkylborates are shown in reactions 10 and 11; the latter route offers advantages in cases where the

[5] E. Negishi, *J. Organometallic Chem.*, 1976, **108**, 281.
[6] K. Utimoto, K. Uchida, and H. Nozaki, *Tetrahedron Letters*, 1973, 4527.
[7] A. Pelter, T. W. Bentley, C. R. Harrison, C. Subrahmanyan, and R. J. Laub, *J.C.S. Perkin I*, 1976, 2419.
[8] P. Binger, G. Benedikt, G. W. Rotermund, and R. Köster, *Annalen*, 1968, **717**, 21.
[9] H. C. Brown, A. B. Levy, and M. M. Midland, *J. Amer. Chem. Soc.*, 1975, **97**, 5017.
[10] M. M. Midland, J. A. Sinclair, and H. C. Brown, *J. Org. Chem.*, 1974, **39**, 731.
[11] K. Utimoto, Y. Yabuki, K. Okada, and H. Nozaki, *Tetrahedron Letters*, 1976, 396.

$$[R_3\bar{B}{-}C{\equiv}CH]\,Li^+ \xrightarrow[THF,\,-78°C]{Bu^n\,Li} [R_3\bar{B}{-}C{\equiv}CLi]\,Li^+ \xrightarrow[\substack{THF\text{–}HMPA\\-78°C\text{ to r.t.}}]{R^1X} [R_3\bar{B}{-}C{\equiv}CR^1]\,Li^+ \qquad (10)$$

$$NaR^1{}_3BH + HC{\equiv}CR^2 \xrightarrow{Hexane,\ r.t.} [R^1{}_3\bar{B}{-}C{\equiv}CR^2]\,Na^+ \qquad (11)$$

presence of base-labile groups precludes preparation of the alkynyl-lithium or sodium reagents.

Disodium bis(trialkylborate) salts are prepared in high yield by reaction of ethyne with sodium trialkylborohydrides in benzene (reaction 12),[8]

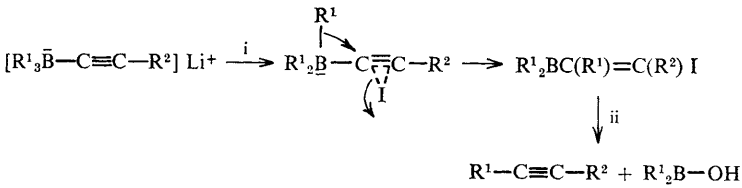
$$2NaR_3BH + HC{\equiv}CH \xrightarrow{PhH,\ r.t.} [R_3\bar{B}{-}C{\equiv}C{-}\bar{B}R_3]\,2Na^+ \qquad (12)$$

while sodium trialkylcyanoborates are readily prepared by reaction of trialkylboranes with sodium cyanide (reaction 13).[12]

$$R_3B + NaCN \xrightarrow{THF,\ r.t.} [R_3\bar{B}{-}CN]\,Na^+ \qquad (13)$$

3 Synthesis of Alkynes

In general, the synthetic approach to alkynes involves treatment of the alkynylborate with a suitable electrophilic reagent, thereby promoting migration of an organo-group from boron to carbon; the intermediate alkenylborane then undergoes either spontaneous or base-induced elimination of an organoborane species to yield the alkyne. The most commonly used electrophilic reagent is iodine, and the procedure is illustrated in Scheme 1.



Reagents: i, I_2; ii, NaOH

Scheme 1

Monoynes.—The procedure outlined in Scheme 1 has been applied to the synthesis of internal alkynes (reaction 14).[13]

$$[R^1{}_3\bar{B}{-}C{\equiv}C{-}R^2]\,Li^+ \xrightarrow{I_2,\ Et_2O,\ -78°C} R^1{-}C{\equiv}C{-}R^2\ (>90\%) \qquad (14)$$

[12] A. Pelter, K. Smith, M. G. Hutchings, and K. Rowe, *J.C.S. Perkin I*, 1975, 129.
[13] A. Suzuki, N. Miyaura, S. Abiko, M. Itoh, H. C. Brown, J. A. Sinclair, and M. M. Midland, *J. Amer. Chem. Soc.*, 1973, **95**, 3080.

Terminal alkynes ($R^2 = H$) are likewise prepared in 75—94% yields from the corresponding ethynylborates,[10] while 2-chloroethynylborates give symmetrical alkynes (reaction 15).[14]

$$[R_3\bar{B}—C\equiv C—Cl]\,Li^+ \xrightarrow{I_2,\ THF,\ -78°C} R—C\equiv C—R \quad (48—78\%) \qquad (15)$$

The use of methanesulphinyl chloride in place of iodine gives an intermediate alkenylborane which undergoes spontaneous elimination (reaction 16).[15]

$$[R^1{}_3\bar{B}—C\equiv C—R^2]\,Li^+ \xrightarrow{MeSOCl} R^1{}_2BC(R^1){=}C(R^2)SOMe \rightarrow R^1—C\equiv C—R^2 + R^1{}_2BSOMe \quad (55—82\%) \qquad (16)$$

Attempts to achieve selective alkyl group migration by use of *B*-alkyl-9-borabicyclo[3,3,1]nonane or dialkylthexylborane (thexyl = 2,3-dimethyl-2-butyl) derivatives unfortunately gives mixtures of products resulting from random migration.[15] While migration of the *B*-cyclo-octyl moiety has been observed in organoborane reactions,[16] competitive migration of the bulky thexyl group has not previously been reported.

Diynes.—Reaction of dicyclohexyl- or disiamyl-chloroboranes (siamyl = 3-methyl-2-butyl) with two mole equivalents of an alkynyl-lithium furnishes the corresponding dialkyldialkynylborates which, on treatment with iodine, give symmetrical conjugated diynes (reaction 17).[17]

$$R^1{}_2BCl + 2LiC\equiv C—R^2 \xrightarrow{THF} [R^1{}_2\bar{B}(C\equiv CR^2)_2]\,Li^+ \xrightarrow{I_2,\ -78°C} R^2—C\equiv C—C\equiv C—R^2 \quad (70—90\%) \qquad (17)$$

$(R^1 = c\text{-}C_6H_{11}$ or $Me_2CHCHMe)$

Attempted synthesis of unsymmetrical dialkynylborates by sequential reaction of dialkylchloroboranes with two different alkynyl-lithium reagents failed owing to preferential formation of the symmetrical dialkynylborate during the first addition.[18] This difficulty was, however, overcome by replacement of the dialkylchloroborane by the dialkylmethylthioborane which gives the initial dialkylalkynylborane stabilized as the methylthio-complex; further reaction with the second alkynyl-lithium reagent then proceeds *via* dissociation of the complex to the active dialkylalkynylborane as shown in Scheme 2.[18]

[14] K. Yamada, N. Miyaura, M. Itoh, and A. Suzuki, *Tetrahedron Letters*, 1975, 1961.
[15] M. Naruse, K. Utimoto, and N. Nozaki, *Tetrahedron*, 1974, **30**, 2159.
[16] Reference 3, p. 258.
[17] A. Pelter, K. Smith, and M. Tabata, *J.C.S. Chem. Comm.*, 1975, 857.
[18] A. Pelter, R. Hughes, K. Smith, and M. Tabata, *Tetrahedron Letters*, 1976, 4385.

$$(c\text{-}C_6H_{11})_2BSMe \xrightarrow{i} [(c\text{-}C_6H_{11})_2B(\bar{C}{\equiv}CR^1)(SMe)]\,Li^+ \rightleftarrows LiSMe +$$

$$(c\text{-}C_6H_{11})_2B{-}C{\equiv}C{-}R^1 \xrightarrow{ii} [(c\text{-}C_6H_{11})_2\,B(C{\equiv}CR^1)(\bar{C}{\equiv}CR^2)]\,Li^+$$

$$\xrightarrow{iii} R^1{-}C{\equiv}C{-}C{\equiv}C{-}R^2\ (51{-}61\%)$$

Reagents: i, $LiC{\equiv}CR^1$, THF, −78 °C; ii, $LiC{\equiv}CR^2$, −78 °C; iii, I_2, −78 °C

Scheme 2

An alternative route to unsymmetrical conjugated diynes involves formation of the methoxy-stabilized dialkylalkynylborane complex.[19] While the overall yields of diynes are slightly higher than those obtained using the methylthio-complex, this method suffers from the disadvantage that the reactive dialkyl-alkynylborane is only freed for further reaction on treatment with boron trifluoride (Scheme 3).

$$Sia_2BOMe \xrightarrow{i} [Sia_2\bar{B}{-}C{\equiv}CR^1(OMe)]\,Li^+ \xrightarrow{ii} Sia_2B{-}C{\equiv}C{-}R^1 \xrightarrow{iii}$$

$$[Sia_2\bar{B}(C{\equiv}CR^1)(C{\equiv}CR^2)]\,Li^+ \xrightarrow{iv} R^1{-}C{\equiv}C{-}C{\equiv}C{-}R^2$$

(Sia = $Me_2CHCHMe$) (61—73%; g.l.c. yields)

Reagents: i, $LiC{\equiv}CR^1$, THF, −78 °C; BF_3, Et_2O, THF, −78 °C—25 °C; iii, $LiC{\equiv}CR^2$, −78 °C; iv, I_2, −78 °C

Scheme 3

Enynes.—A similar approach to that used in the synthesis of conjugated diynes has been applied to the synthesis of conjugated *trans*-enynes as shown in Scheme 4.[20]

$$Sia_2BH + HC{\equiv}CR^1 \xrightarrow{i} Sia_2BCH{=}\overset{E}{C}HR^1 \xrightarrow{ii} [Sia_2\bar{B}(CH{=}CHR^1)(C{\equiv}CR^2)]Li^+$$

$$\xrightarrow{iii,\ iv} R^1CH{=}CH{-}C{\equiv}C{-}R^2\ (60{-}74\%;\ >\ 99\%E)$$

Reagents: i, THF, 0 °C; ii, $LiC{\equiv}CR_2$, THF, −50 °C; iii, I_2, THF, −78 °C—25 °C; iv, NaOH

Scheme 4

The method has been successfully applied to the synthesis of the pheremones, bombykol (1)[20] and (7*E*, 9*Z*)-dodecadienyl-1-yl acetate (2).[21]

[19] J. A. Sinclair and H. C. Brown, *J. Org. Chem.*, 1976, **41**, 1078.
[20] E. Negishi, G. Lew, and T. Yoshida, *J.C.S. Chem. Comm.*, 1973, **874.**
[21] E. Negishi and A. Abramovitch, *Tetrahedron Letters*, 1977, 411.

$$HO(CH_2)_9CH\overset{E}{=}CH—CH\overset{Z}{=}CH—C_3H_7\text{-}n \qquad EtCH\overset{Z}{=}CH—CH\overset{E}{=}CH(CH_2)_6OAc$$

(1) (2)

The efficiency of the alkynylborate synthetic approach is highlighted by the fact that the overall yield of (2) obtained was 40% (>98% pure), compared with a yield of 10% (~80% pure) obtained in an earlier synthesis.[22]

Application of the above method to the synthesis of *cis*-enynes is not as efficient, only proceeding in yields of 30—50% because of competitive migration of the siamyl group.[23]

4 Synthesis of Alkenes

The conversion of alkynylborates into alkenes *via* electrophilic attack and protonolysis of the intermediate alkenylborane has been thoroughly investigated by a number of groups. In general, mixtures of the *E* and *Z* stereoisomers are obtained, but the stereoselectivity of the boron to carbon alkyl group migration has been found to be high in a number of cases. The transformation of alkynylborates to alkenes thus constitutes a valuable addition to the many methods available for the stereoselective synthesis of alkenes.[24]

Terminal Alkenes.—Protonation of the ethylenediamine-stabilized complexes of ethynylborates (reaction 9) with propanoic acid gives monosubstituted alkenes (reaction 18),[25] while treatment of the intermediate alkenylborane with iodine and base gives the corresponding symmetrical disubstituted alkenes (reaction 19).[9]

$$[R_3\bar{B}—C\equiv CH]\,Li^+,EDA \xrightarrow{EtCO_2H} R—CH=CH_2 \quad (56—64\%) \qquad (18)$$

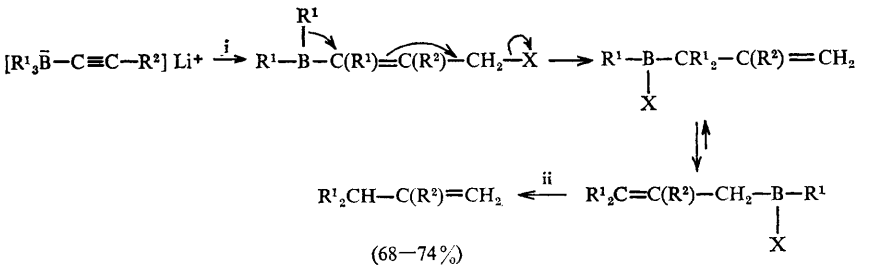
$$[R_3\bar{B}—C\equiv CH]\,Li^+ \xrightarrow[\text{ii, NaOH, } -78°C]{\text{i, HCl, THF, } -78°C} R_2B—C(R)=CH_2 \xrightarrow[NaOH]{I_2}$$

$$R_2C=CH_2 \quad (76\%\ R = c;\ C_6H_{11}) \qquad (19)$$

$$R_3B + Li—CMe=CH_2 \rightarrow [R_3\bar{B}—CMe=CH_2]\,Li^+$$

Unsymmetrical disubstituted alkenes may be prepared *via* alkylation with dihalogenomethanes, followed by protonolysis (Scheme 5).[26]

[22] J. N. Labovitz, C. A. Hendrick, and V. L. Corbin, *Tetrahedron Letters*, 1975, 4209.
[23] E. Negishi, R. M. Williams, G. Lew, and T. Yoshida, *J. Organometallic Chem.*, 1975, **92**, C4.
[24] J. Reucroft and P. G. Sammes, *Quart. Rev.*, 1971, **25**, 135.
[25] N. Miyaura, T. Yoshinari, M. Itoh, and A. Suzuki, *Tetrahedron Letters*, 1974, 2961.
[26] A. Pelter and C. R. Harrison, *J.C.S. Chem. Comm.*, 1974, 828.



Reagents: i, CH_2X_2, DG, 0 °C; ii, Pr^iCO_2H

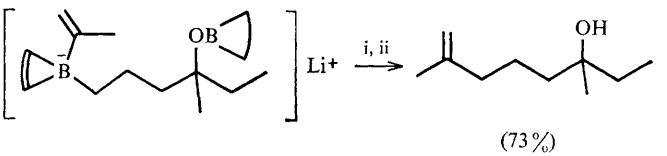
Scheme 5

Iodination of trialkylisopropenylborates, followed by oxidation, provides a novel synthetic route to terpenoids (reaction 20).[27]

$$R_3B + LiCMe{=}CH_2 \rightarrow [R_3\bar{B}{-}CMe{=}CH_2]\,Li^+$$

$$\xrightarrow[\text{ii, } H_2O_2,\ OH^-]{\text{i, } I_2,\ -78\,^\circ C \text{ to } 0\,^\circ C} R{-}CMe{=}CH_2 \quad (73{-}100\%) \qquad (20)$$

The selective transfer of an alkyl group from the corresponding *B*-alkyl-9-borabicyclo[3,3,1]nonane borate derivatives greatly enhances the synthetic utility of the method (Scheme 6).[27]



Reagents: i, I_2, −78 °C—0°C; ii, H_2O_2, OH^-

Scheme 6

Disubstituted Internal Alkenes.—Protonation of alkynylborates generally gives mixtures of the *E* and *Z* stereoisomers,[8] though the ratio of stereoisomers has been found to be dependent on the acid used as the proton source. Thus, with methanesulphonic acid the *E*-alkene predominates,[28] whereas with propanoic acid the *Z*-alkene is preferentially formed.[25] Another interesting feature of the reaction is the marked effect exerted by the presence of a phenyl group, either in the alkyne moiety[25] or as the migrating group.[28] In both these cases the *Z*-alkene is predominantly formed (reactions 21 and 22).

[27] N. Miyaura, H. Tagami, M. Itoh, and A. Suzuki, *Chem. Letters*, 1974, 1411.
[28] A. Pelter, C. R. Harrison, C. Subrahmanyan, and D. Kirkpatrick, *J.C.S. Perkin I*, 1976, 2435.

$$[Bu^n{}_3\bar{B}{-}C{\equiv}C{-}Ph]\,Li^+ \xrightarrow{EtCO_2H,\ -78\,^\circ C} Bu^nCH{=}CHPh \quad (81\%;\ 98\%\ Z) \qquad (21)$$

$$[Ph_3\bar{B}{-}C{\equiv}C{-}Bu^n]\,Li^+ \xrightarrow[ii.\ HOAc]{i,\ MeSO_3H,\ DG,\ 0^\circ C} PhCH{=}CHBu^n \quad (81\%,\ 98\%\ Z) \qquad (22)$$

Protonation of dialkylalkynylthexylborates gives a predominance of the *E*-alkene irrespective of whether methanesulphonic or propanoic acid is used as proton source (reaction 23).[28]

$$[(Me_2CHCMe_2)\bar{B}R^1{}_2(C{\equiv}CR^2)]\,Li^+ \xrightarrow[ii,\ RCO_2H]{i,\ H^+} R^1CH{=}CHR^2 \quad (>70\%\ E) \qquad (23)$$

For the phenylalkynylmoiety (R^2 = Ph), however, the *Z*-alkene predominates to an extent exceeding 95%.[28]

Stereospecific synthesis of *Z*-alkenes has been achieved using dialkylchloroboranes[29] or tributyltin chloride[30] as the electrophilic reagents (reactions 24 and 25).

$$[R^1{}_3\bar{B}{-}C{\equiv}C{-}R^2]\,Na^+ \xrightarrow[THF]{ClBR^3{}_2} R^1{}_2B{-}C(R^1){=}C(R^2)BR^3{}_2 \xrightarrow{H_2O}$$

$$R^1CH{=}CHR^2 \quad (65{-}81\%;\ Z\ \text{only}) \qquad (24)$$

$$[R_3{}^1\bar{B}{-}C{\equiv}C{-}R^2]\,Li^+ \xrightarrow{Bu^n{}_3SnCl} R^1{}_2B{-}C(R^1){=}C(R^2)SnBu^n{}_3 \xrightarrow{HCO_2H}$$

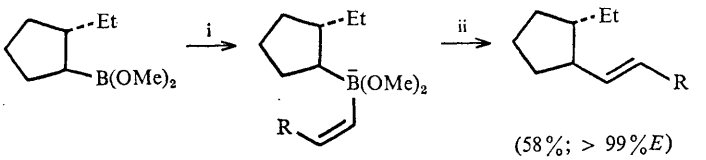
$$R^1CH{=}CHR^2 \quad (70{-}79\%;\ Z\ \text{only}) \qquad (25)$$

The stereoselective synthesis of *E*-alkenes by reaction of bis(trialkyl) ethynylborates with one mole equivalent of cyanogen bromide proceeds with double migration of alkyl groups (reaction 26).[31]

$$[R_3\bar{B}{-}C{\equiv}C{-}\bar{B}R_3]\,2Li^+ \xrightarrow[NaOMe,\ r.t.]{BrCN,\ Et_2O} RCH{=}CHR \quad (46{-}88\%;\ E) \qquad (26)$$

The application of alkenylborates to the synthesis of internal alkenes has been elegantly demonstrated in studies related to prostaglandin synthesis.[32] The reaction sequence involves iodination of an intermediate boronic ester as shown in Scheme 7.

[29] P. Binger and R. Köster, *Tetrahedron Letters*, 1965, 1901.
[30] J. Hooz and R. Mortimer, *Tetrahedron Letters*, 1976, 805.
[31] N. Miyaura, S. Abiko, M. Itoh, and A. Suzuki, *Synthesis*, 1975, 669.
[32] D. A. Evans, T. C. Crawford, R. C. Thomas, and J. A. Walker, *J. Org. Chem.*, 1976, **41**, 3947.



(58%; > 99%*E*)

R = CH(OTHP)(n-C_5H_{11}); THP = Tetrahydropyranyl

Reagents: i, *Z*-LiCH=CHR, THF, −45 °C; ii, I_2, NaOMe, MeOH–THF

Scheme 7

Use of the *E*-lithioalkene gives the corresponding *Z*-cyclopentylalkene in 75% yield.[32]

Trisubstituted Alkenes.—The reaction of sodium trialkylalkynylborates with a variety of alkylating agents has been found to give, after hydrolysis, mixtures of *E*- and *Z*-alkenes (reaction 27).[8,29]

$$[R^1{}_3\bar{B}—C\equiv C—R^2]\,Na^+ \xrightarrow[\text{ii, } H_2O]{\text{i, El}^+} R^1CH=CR^2R^3 \quad (E:Z \sim 65:35) \quad (27)$$

$$(El^+ = R^3X,\ R^3OTs,\ Et_3O^+\,BF_4^-)$$

A detailed investigation of the reaction of lithium and sodium trialkylalkynylborates with a variety of alkylating agents indicated that the *E* to *Z* stereoisomeric ratio (~65 : 35) is insensitive to the alkylating agent used, the nature of the solvent, and the counter cation present.[7] As observed in the case of disubstituted alkene synthesis (reactions 21 and 22), the presence of a phenyl group in the borate intermediate greatly enhances the stereoselectivity of the reaction, the *E*-stereoisomer being preferentially formed to an extent exceeding 82%.[7]

The reaction of dialkylalkynylthexylborates proceeds with greatly increased stereoselectivity, but, once again, the *E*:*Z* stereoisomeric ratio varies little with the nature of the alkylating agent or solvent (reaction 28).[7]

$$[(Me_2CHCMe_2)\bar{B}R^1{}_2(C\equiv CR^2)]\,Li^+ \xrightarrow[\text{ii, } Pr^iCO_2H]{\text{i, El}^+,\ DG,\ -78^\circ C} R^1CH=CR^2R^3$$

(55—88%; > 83% R^1, R^3 *cis*) (28)

(El$^+$ = Me_2SO_4, $Et_3O^+BF_4^-$, R^3I, allyl or $PhCH_2Br$; R^3 = alkyl, allyl, $PhCH_2$)

The major stereoisomer formed in each case is that in which the migrating group (R^1) and the group introduced from the alkylating agent (R^3) are *cis* to one another. In no instance was migration of the thexyl group observed, though it should

be noted that the use of groups other than n-alkyl groups (R^1) in the dialkylthexyl moiety was not reported.

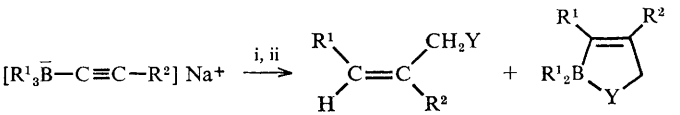
A valuable extension of the above reaction involves the use of α-bromo-ketones and -esters, iodoacetonitrile, and prop-2-ynyl bromide as alkylating agents (reaction 29).[33]

$$[R^1{}_3\bar{B}{-}C{\equiv}C{-}R^2]\,Li^+ + XCH_2Y \xrightarrow[\text{ii, HOAc}]{\text{i, DG, } -78\,^\circ C \text{ to r.t.}} R^1CH{=}C(R^2)CH_2Y \quad (29)$$

(64—77%; R^1, CH_2Y *cis*)

(X = Br or I; Y = COMe, COPh, CO_2Et, CN, C≡CH)

The reaction proceeds in a stereospecific manner with all the reagents indicated (except α-bromo-esters for which 88—96% stereoselectivity is observed) to give products in which the migrating group (R^1) and the alkylating group (CH_2Y) are *cis* to one another. The stereoselectivity of the reaction with α-bromo-esters is increased to >98% when dialkylalkynylthexylborates are used.[33] Similar routes to allylic amines[34] and methyl ethers[35] have been reported. While equimolar mixtures of *E* and *Z* stereoisomers are obtained in both cases, the corresponding *Z*-alkenylboranes are selectively hydrolysed as shown in Scheme 8.



(*Z*) (*E*)

(X = Br; Y = NMe_2; > 90%) (X = Cl; Y = OMe; 45—75%)

Reagents: i, XCH_2Y, Et_2O; ii, H_2O, r.t.

Scheme 8

The unchanged (*E*)-alkenylboranes may be converted into the corresponding allylic derivatives by treatment with triethylaluminium and acid in the case of the amines[34] and acetic acid in the case of the methyl ethers.[35]

The protonation–iodination reaction sequence (reaction 19) has also been applied to the synthesis of trisubstituted alkenes (reaction 30).[28,36]

$$[R^1{}_3\bar{B}{-}C{\equiv}C{-}R^2]\,Li^+ \xrightarrow[-70^\circ C]{HCl,\ THF} R^1{}_2BC(R^1){=}CHR^2 \xrightarrow[MeOH,\ -20^\circ C]{I_2,\ NaOMe}$$

$$R^1{}_2C{=}CHR^2 \quad (64—79\%) \qquad (30)$$

[33] A. Pelter, K. J. Gould, and C. R. Harrison, *J.C.S. Perkin I*, 1976, 2428.
[34] P. Binger and R. Köster, *Chem. Ber.*, 1975, **108**, 395.
[35] P. Binger and R. Köster, *Synthesis*, 1974, 350.
[36] G. Zweifel and R. P. Fisher, *Synthesis*, 1975, 376.

A useful application of procedures discussed this far is illustrated by the synthesis of propylure, the sex attractant of the pink Bollworm moth (Scheme 9).[37]

$$[Pr^n_3\bar{B}{-}C{\equiv}C{-}SiMe_3]\,Li^+ + TsO(CH_2)_2{-}C{\equiv}C{-}(CH_2)_4OTHP \xrightarrow{i,\ ii}$$

$$Pr^n_2BC(Pr^n){=}C(SiMe_3)\,(CH_2)_2{-}C{\equiv}C{-}(CH_2)_4OTHP \xrightarrow{iii}$$

$$Pr^n_2C{=}C(SiMe_3)\,(CH_2)_2{-}C{\equiv}C{-}(CH_2)_4OTHP \xrightarrow{4\ steps}$$

$$Pr^n_2C{=}CH(CH_2)_2CH\overset{E}{=}CH(CH_2)_4OAc$$

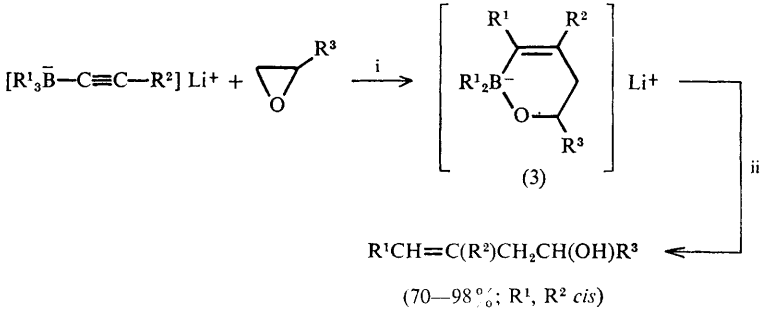
Propylure (30% overall yield)

(THP = Tetrahydropyranyl)

Reagents: i, THF, −78 °C; ii Δ; iii, I_2, NaOH, 0 °C to r.t.

Scheme 9

Epoxides also serve as electrophilic reagents in promoting the transformation of alkynylborates into alkenes; such reactions have been used in an elegant synthesis of hydroxy-alkenes (Scheme 10).[38] Heating the reaction mixture results in exclusive formation of the cyclic borane (3); in dichloromethane or tetrahydrofuran, however, mixtures of *E* and *Z* isomers are formed.[38a] The reaction,



Reagents: i, $\Delta \geqslant 5$ h; ii, HOAc, Δ

Scheme 10

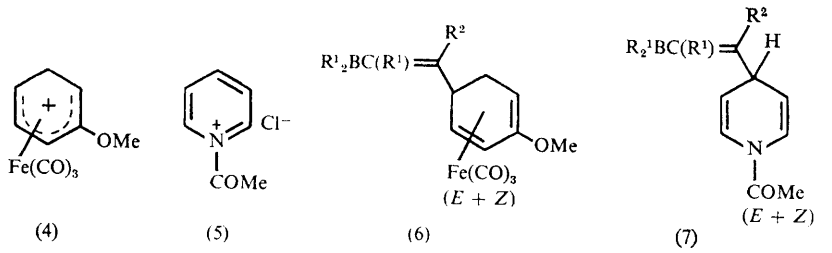
however, proceeds in low yield for more hindered epoxides, such as cyclohexene oxide.[38]

The reaction of acetyl chloride with alkynylborates proceeds *via* double migration of alkyl groups to give, after oxidation, $\alpha\beta$-unsaturated ketones (reaction 31).[39]

[37] K. Utimoto, M. Kitai, M. Naruse, and H. Nozaki, *Tetrahedron Letters*, 1975, 4233.
[38] M. Naruse, K. Utimoto, and H. Nozaki, *Tetrahedron*, 1974, **30**, 3037.
[38a] K. Utimoto, T. Furubayashi, and H. Nozaki, *Chem. Letters*, 1975, 397.
[39] M. Naruse, T. Tomita, K. Utimoti, and H. Nozaki, *Tetrahedron*, 1974, **30**, 835.

$$[R^1_3\bar{B}{-}C{\equiv}C{-}R^2]\,Li^+ \xrightarrow[\text{ii, } CrO_3,\ Me_2CO]{\text{i, MeCOCl, THF, 0°C}} R^1_2C{=}C(R^2)COMe \quad (30\text{–}42\%) \quad (31)$$

Other electrophilic reagents investigated are the cationic metal complex (4)[40] and *N*-acetylpyridinium chloride (5) (Scheme 11).[41] The products are the



(4) (5) (6) (7)

Scheme 11

alkenylborane (6) and 4-alkenyl-substituted-1,4-dihydro-pyridines (7) respectively. Trisubstituted alkenes have also been prepared by the reaction of bis(trialkyl)-ethynylborates with a 2: 3 molar ratio of cyanogen bromide (reaction 32).[31]

$$[R_3\bar{B}{-}C{\equiv}C{-}\bar{B}R_3]\,2Li^+ \xrightarrow[\text{ii, } EtCO_2H]{\text{i, 2BrCN, } Et_2O,\ NaOMe,\ r.t.} R_2C{=}CHR \quad (50\text{–}76\%)\ (32)$$

The synthetic utility of this reaction appears to be limited by the formation of significant amounts of di- (reaction 26) and tetra-substituted alkenes as by-products.

Highly stereoselective routes to trimethylsilylalkenylboranes are illustrated in reactions (33)[42] and (34).[43]

$$[Et_3\bar{B}{-}C{\equiv}C{-}Me]\,Na^+ \xrightarrow[Et_2O,\ 0\text{–}10\ °C]{ClSiMe_3} Et_2BC(Et){=}C(Me)SiMe_3 \quad (33)$$

(62%; Et, Me *cis*)

$$[Et_3\bar{B}{-}C{\equiv}C{-}SiMe_3]\,Li^+ \xrightarrow{El^+} Et_2BC(Et){=}C(R)SiMe_3 \quad (34)$$

(63—87%; 88—96% Et, R *cis*)

($El^+ = ClCH_2OMe,\ ICH_2NMe_2,\ Et_3O^+BF_4^-,\ ClSiMe_3$)

(R = CH_2OMe, CH_2NMe_2, Et, $SiMe_3$)

The ready conversion of the trimethylsilyl group into other functional groups enhances the synthetic utility of these processes.

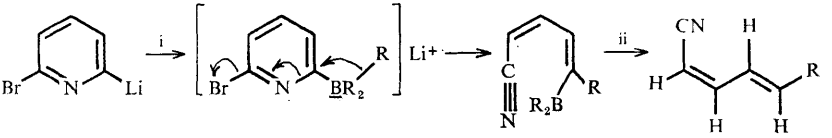
[40] A. Pelter, K. J. Gould, and L. A. P. Kane-Maguire, *J.C.S. Chem. Comm.*, 1974, 1029.
[41] A. Pelter and K. J. Gould, *J.C.S. Chem. Comm.*, 1974, 347.
[42] P. Binger and R. Köster, *Synthesis*, 1973, 309.
[43] R. Köster and L. A. Hagelee, *Synthesis*, 1976, 118.

Tetrasubstituted Alkenes.—Reaction of bis(trialkyl)ethynylborates with a three molar ratio of cyanogen bromide gives low yields of tetrasubstituted alkenes, together with large amounts of trisubstituted alkenes (reaction 32), the former only being formed with primary alkyl groups, whereas the cyclic intermediates (3; Scheme 10), formed in the reaction of alkynylborates with epoxides, react, with iodine to give alkenyliodides (reaction 35).[38]

(3; R^1 = Bu^n, R^2 = n-C_5H_{11}, R^3 = Et) $\xrightarrow[\text{ii, } I_2\text{, NaOH}]{\text{i, } \Delta(-R^1Li)}$
(see Scheme 10)

$$R^1C(I)=C(R^2)CH_2CH(OH)R^3 \quad (71\%;\ R^1, R^2\ cis) \qquad (35)$$

Dienes.—2-Bromo-6-lithiopyridine readily reacts with trialkylboranes with stereospecific cleavage of the pyridine ring to give conjugated dienylnitriles as shown in Scheme 12.[44] Treatment of the intermediate dienylborane with iodine



(60—93%; R = alkyl)

Reagents: i, R_3B,Et_2O; ii, HOAc

Scheme 12

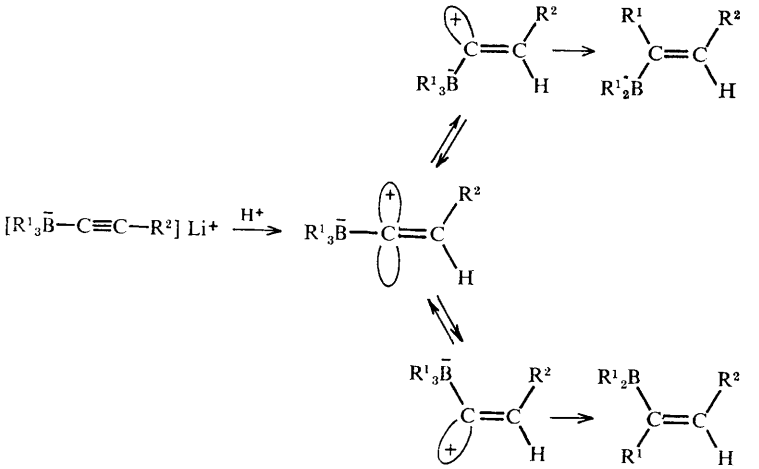
and base gives the dienylnitrile, R_2C=CH—CH=CHCN, in 50—67% yields.[44]

Mechanism and Stereochemistry of Alkene Formation.—The results discussed in the foregoing sections clearly indicate that the formation of alkenes is, in general, not stereospecific. This observation rules out the possibility of the trans-formations occurring by a concerted mechanism involving the migrating group and incoming electrophile being stereospecifically *trans* to one another. In fact, careful studies by Pelter *et al.* have shown that the stereochemistry of the major alkene formed in the alkylation of trialkylalkynylborates is that requiring the *cis* arrangement of the migrating group and the incoming alkyl group (reactions 28 and 29).[7,33]

A mechanism involving the initial formation of a linear vinyl cation which is in equilibrium with two possible sp^2-hybridized vinyl cations has been proposed by Suzuki *et al.* for the protonation of alkynylborates (Scheme 13).[25]

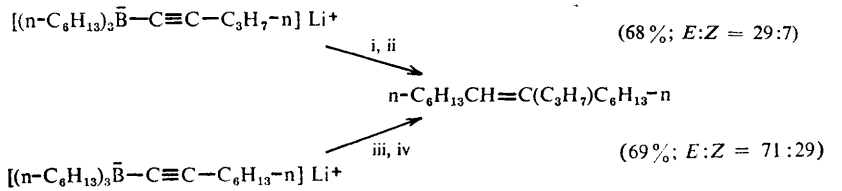
This general mechanism does not, however, account for the influence of a thexyl (reaction 23) or a phenyl group (reactions 21 and 22) on the stereo-chemistry of the reaction, nor for the effect of the nature of the acid used in the protonation step.[25,28] In addition, conclusive evidence that the alkylation of

[44] K. Utimoto, N. Sakai, M. Obayashi, and H. Nozaki, *Tetrahedron*, 1976, **32**, 769.



Scheme 13

alkynylborates proceeds *via* a largely kinetically controlled process has been presented (Scheme 14).[7]



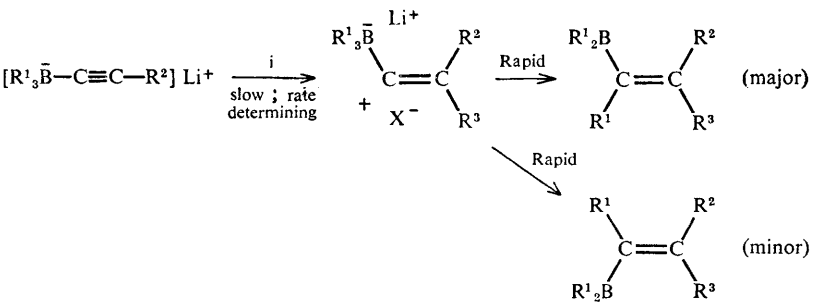
Reagents: i, n-$C_6H_{13}I$, THF; ii, H^+; iii, n-C_3H_7I, THF; iv, H^+

Scheme 14

Equilibration *via* a common vinyl cation species should lead to the same mixture of products from each reaction in Scheme 14. Thermodynamic control is thus clearly ruled out for the alkylation process; in addition, the stereochemistry is found to be insensitive to the nature of the solvent, the counterion, and the alkylating reagent used, but the rate of reaction is strongly influenced by the alkylating reagent.

A two-stage mechanism involving rate-determining attack on the alkynyl moiety to give a bent vinyl cationic intermediate, which undergoes rapid exothermic rearrangement with preferred retention of stereochemistry at the migration terminus, has been proposed to account for the above observations (Scheme 15).[7]

Although the intermediate is formally represented as a zwitterion, MINDO/3 calculations indicate only small charges on the boron and carbon, thus supporting the non-polar characteristics of the process. Calculations have also indicated



Reagent: i, R^3X

Scheme 15

an increase in stereoselectivity of reaction (with retention of configuration at the migration terminus being favoured) for rearrangements involving bulky substituents on boron, thus supporting the increase in stereoselectivity observed for thexyl derivatives (reaction 28).[7]

5 Synthesis of Ketones

Organoborates have found extensive application in the synthesis of ketones and, of the stable organoborates, cyanoborates were the first to be extensively investigated.[12] Of the electrophilic reagents studied, acylating agents, in particular trifluoroacetic anhydride, proved to be the most effective in promoting migration of groups from boron to carbon (reaction 36).[12]

$$[R_3\bar{B}—CN]\,Na^+ \xrightarrow[\text{ii, } H_2O_2,\ NaOH]{\text{i, } (CF_3CO)_2O,\ DG,\ -78\,^\circ C \text{ to } 0\,^\circ C} R_2CO \quad (84—100\%) \qquad (36)$$

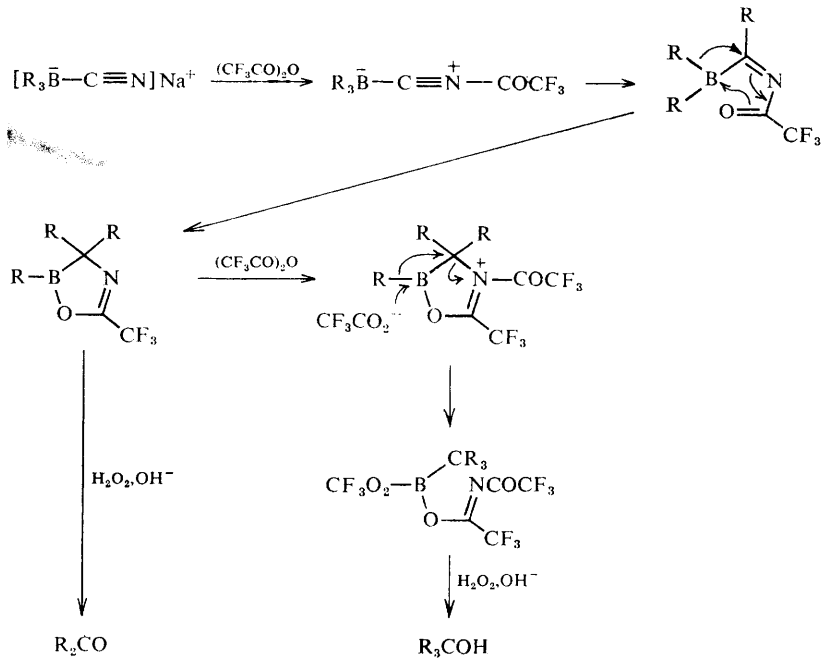
The relative migratory aptitudes of alkyl groups is in the order n > s > t, and migration of groups occurs with complete retention of configuration.[45] Diglyme is found to be superior to tetrahydrofuran as solvent, since some triple migration occurs in the latter solvent to give trialkylmethanols (reaction 39), particularly when tri-n-alkylcyanoborates are used. Unsymmetrical ketones are readily synthesized by use of dialkylcyanothexylborates (reaction 37).[12]

$$ThBH_2 \xrightarrow[\text{ii, Alkene B}]{\text{i, Alkene A}} ThBR_AR_B \xrightarrow[\text{iii, } H_2O_2,\ NaOH]{\text{i, NaCN, THF, r.t.}\ \text{ii, } (CF_3CO)_2O,\ -78 \text{ to } 0\,^\circ C} R_ACOR_B \quad (76—85\%) \qquad (37)$$

(Th = Me_2CHCMe_2)

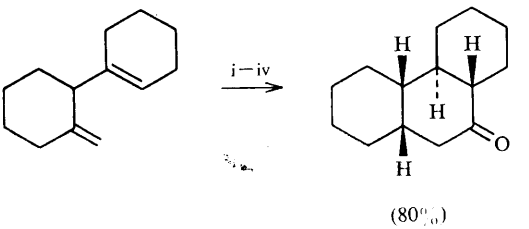
The transformation occurs by the mechanism outlined in Scheme 16.

[45] A. Pelter, M. G. Hutchings, K. Smith, and D. J. Williams, *J.C.S. Perkin I*, 1975, 145.



Scheme 16

A most useful application is the ready synthesis of fused ring systems (Scheme 17).[12]



Reagents: i, $ThBH_2$, THF, 0°C; ii, KCN, r.t.; iii, $(CF_3CO)_2O$, −78°C to r.t.; iv, H_2O_2, NaOH

Scheme 17

Use of acids as the electrophilic reagents generally gives inferior yields of ketones.[46]

[46] A. Pelter, M. G. Hutchings, and K. Smith, *J.C.S. Perkin I*, 1975, 142.

Oxidation of the intermediate alkenylboranes obtained upon treatment of alkynylborates with suitable electrophilic reagents (Scheme 15) gives ketones in high yields. Alkynylborates thus constitute extremely valuable intermediates in the synthesis of a wide variety of ketones (reaction 38).

$$[R^1{}_3\bar{B}{-}C{\equiv}C{-}R^2] \xrightarrow{El^+} \underset{(E+Z)}{R^1{}_2B{-}C(R^1){=}C(R^2)El} \xrightarrow[NaOH]{H_2O_2} R^1COCH(R^2)El \quad (38)$$

Thus, many of the reactions discussed in Section 4 on the synthesis of alkenes have also been applied to the synthesis of ketones. Some results of these studies are given in the Table.

Table *Conversion of alkynylborates into ketones (reaction 38)*

Electrophilic reagent El^+	*Ketone*[a] $R^1COCH(R^2)El$	*Yield* %	*Ref.*
HCl	R^1COMe[b]	70—90	9
$MeSO_3H$	$R^1COCH_2R^2$	78—86	28
$Bu^n{}_3SnCl$	$R^1COCH_2R^2$[c]	88	30
MeOTs	$R^1COCH(Me)R^2$	88—98	7
Me_2SO_4	$R^1COCH(Me)R^2$	81—85	7
$Et_3O^+BF_4^-$	$R^1COCH(Et)R^2$	83—95	7
$CH_2{=}CHCH_2Br$	$R^1COCH(R^2)CH_2CH{=}CH_2$	80—88	7
$PhCH_2Br$	$R^1COCH(R^2)CH_2Ph$	78—81	7
$BrCH_2CO_2Et$	$R^1COCH(R^2)CH_2CO_2Et$	74—78	33
$BrCH_2COMe$	$R^1COCH(R^2)CH_2COMe$	70—75	33
$BrCH_2COPh$	$R^1COCH(R^2)CH_2COPh$[d]	74	33
$BrCH_2C{\equiv}CH$	$R^1COCH(R^2)CH_2C{\equiv}CH$	75—80	33
ICH_2CN	$R^1COCH(R^2)CH_2CN$	62—71	33
	$R^1COCH(R^2)CH_2CH(OH)R^3$[e]	59—95	38

[a] R^1, R^2 = alkyl, cycloalkyl; [b] R^2 = H; [c] R^1 = Et; R^2 = Bu^n; [d] R^1 = R^2 = n-C_6H_{13}; [e] R^2, R^3 = alkyl, aryl.

The results listed in Table 1 serve to illustrate the tremendous synthetic utility of these reactions. Groups R^1, R^2, and El (reaction 38) all originate from simple and independent units which can be varied to give a wide range of products. A particularly valuable aspect of the reaction is the potential to achieve regiospecific α-substitution of a ketone, $R^1COCH_2R^2$, by a group El whether it be alkyl, allyl, benzyl or any of the other groups listed in Table 1.

6 Synthesis of Alcohols

As in the synthesis of ketones (Section 5), cyanoborates were the first of the stable organoborates to be applied to the synthesis of alcohols.[47] Treatment

[47] A. Pelter, M. G. Hutchings, K. Rowe, and K. Smith, *J.C.S. Perkin I*, 1975, 138.

with excess trifluoroacetic anhydride promotes migration of three groups from boron to carbon (Scheme 16; reaction 39).

$$[R_3\bar{B}—CN]\,K^+ \xrightarrow[\text{ii, } H_2O_2,\ NaOH]{\text{i, Excess } (CF_3CO)_2O,\ DG,\ 0—40^\circ C} R_3COH\ (60—90\%) \qquad (39)$$

Ready transfer of n-alkyl group occurs, while migration of s- and t-alkyl groups is accelerated by the addition of 10% pyridine to the reaction mixture.[47]

The use of alkenyl- and alkynyl-borates is illustrated in reactions (40),[9,48] (41),[49] and (42).[50]

$$[R^1_3\bar{B}—C\equiv C—R^2]\,Li^+ \xrightarrow[THF,\ \Delta]{HCl\text{-}H_2O} R^1B(OH)—CR^1_2CH_2R^2 \xrightarrow[NaOH]{H_2O_2}$$

$$R^1_2C(OH)CH_2R^2\ \ (30—86\%) \qquad (40)$$

$$R^1—C\equiv C—R^2 \xrightarrow[THF]{R^3_2BH} R^1CH=C(R^2)BR^3_2 \xrightarrow[70\,^\circ C]{MeLi} [R^1CH=C(R^2)\bar{B}R^3_2Me]\,Li^+$$

$$\xrightarrow[Et_2O]{HCl} R^1CH_2C(BR^3Me)R^2R^3 \xrightarrow[NaOH]{H_2O_2} R^1CH_2C(OH)R^2R^3\ \ (69—76\%) \qquad (41)$$

$$R_3B + CH_2=C(Li)OMe \xrightarrow[-80\,^\circ C \text{ to r.t.}]{THF} [CH_2=C(R)\bar{B}R_2OMe]\,Li^+ \xrightarrow[r.t.]{2M\text{-}HCl} \qquad (42)$$

$$MeC(BROMe)R_2 \xrightarrow[NaOH]{H_2O_2} MeC(OH)R_2\ \ (87—100\%)$$

1,4-Diols may be synthesized by reaction of alkenylborates with epoxides as shown in reaction (43).[6]

$$[R^1_3\bar{B}—CH=CH_2]\,Li^+ + \underset{R^2}{\overset{O}{\triangle}} \xrightarrow[\text{ii, } H_2O_2,\ NaOH]{\text{i, } Et_2O,\ r.t.} R^1CH(OH)CH_2CH_2CH(OH)R^2$$

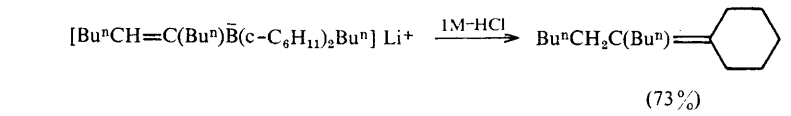
$$(90—100\%) \qquad (43)$$

7 Protonation, Protonolysis, or Dehydroboration?

Treatment of alkynylborates with organic acids (reactions 21 and 22) gives alkenylboranes which may be treated further as desired. Similar results are obtained on treatment with aqueous acid at −78 °C (reaction 19), but at higher temperatures further protonation and rearrangement of the alkenylborane occurs (reaction 40). On reaction with *anhydrous acid* (HCl), alkenylboranes undergo protonolysis to give alkenes;[49] alkenylborates, however, undergo protonation and rearrangement to give trialkylboranes, which may react further (reaction 41). Treatment of alkenyldialkylmethoxyborates with *aqueous*

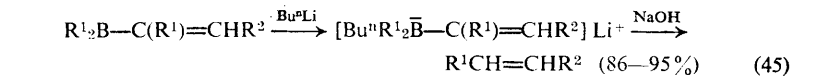
[48] M. M. Midland and H. C. Brown, *J. Org. Chem.*, 1975, **40**, 2845.
[49] G. Zweifel and R. P. Fisher, *Synthesis*, 1974, 339.
[50] A. B. Levy and S. J. Schwartz, *Tetrahedron Letters*, 1976, 2201.

acid also results in protonation and rearrangement (reaction 42); in the case of alkenyltrialkylborates, however, protonation–rearrangement is followed by rapid dehydroboration to give alkenes (reaction 44).[51,52]



(44)

In general, base treatment of alkenyltrialkylborates gives the corresponding alkenes, thus providing a useful alternative to the normal protonolysis procedure of treatment of alkenylboranes with carboxylic acids (reaction 45).[52]



(45)

The above results clearly indicate that care must be exercised to controlling the conditions of reaction when using acids.

8 Why Organoboron Derivatives?

The synthetic versatility of organoboranes has been amply demonstrated;[2–4] organoborates clearly possess equal promise. What properties give organoboron compounds such unique potential in organic synthesis?

Their relative unreactivity to many functional groups compared with other organometallic reagents, such as Grignard and alkyl-lithium compounds.

The ready synthesis of organoboranes of differing structures.[53] In this respect, the tolerance of many functional groups by the hydroboration reaction permits the synthesis of organoboranes and organoborates containing a wide variety of functionalities.

The complete retention of configuration during the transfer of asymmetric groups in reactions proceeding by ionic co-ordination mechanisms.

The broad scope of the reactions. Most of the reactions discussed in the foregoing article proceed in high yield with compounds containing alkyl, cycloalkyl, and aryl groups. Low yields resulting from the transfer of only one of the R groups from a R_3B moiety may often be overcome by use of *B*-alkyl-9-borabicyclo[3,3,1]nonane or dialkylthexylborane (thexyl = Me_2CHCMe_2) derivatives in which selective transfer of the alkyl group is achieved.[54]

With the potential of organoboron compounds in organic synthesis firmly

[51] K.-W. Chiu, E. Negishi, and M. S. Plante, *J. Organometallic Chem.*, 1976, **112**, C3.
[52] E. Negishi and K.-W. Chiu, *J. Org. Chem.*, 1976, **41**, 3484.
[53] K. Smith, *Chem. Soc. Rev.*, 1974, **3**, 443.
[54] Reference 3, Section 8.2.2.

established it is hoped that these compounds will be fully exploited in devising new or improved synthetic routes to complex organic molecules.

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